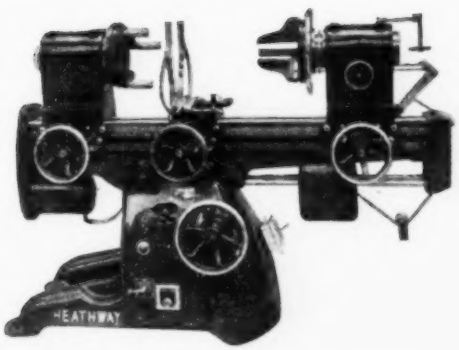
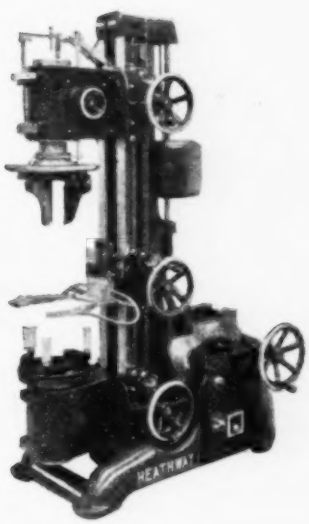
NATURE
A Weekly Journal of Science

Vol. 190, No. 4774 SATURDAY, APRIL 29, 1961 2s. 6d.





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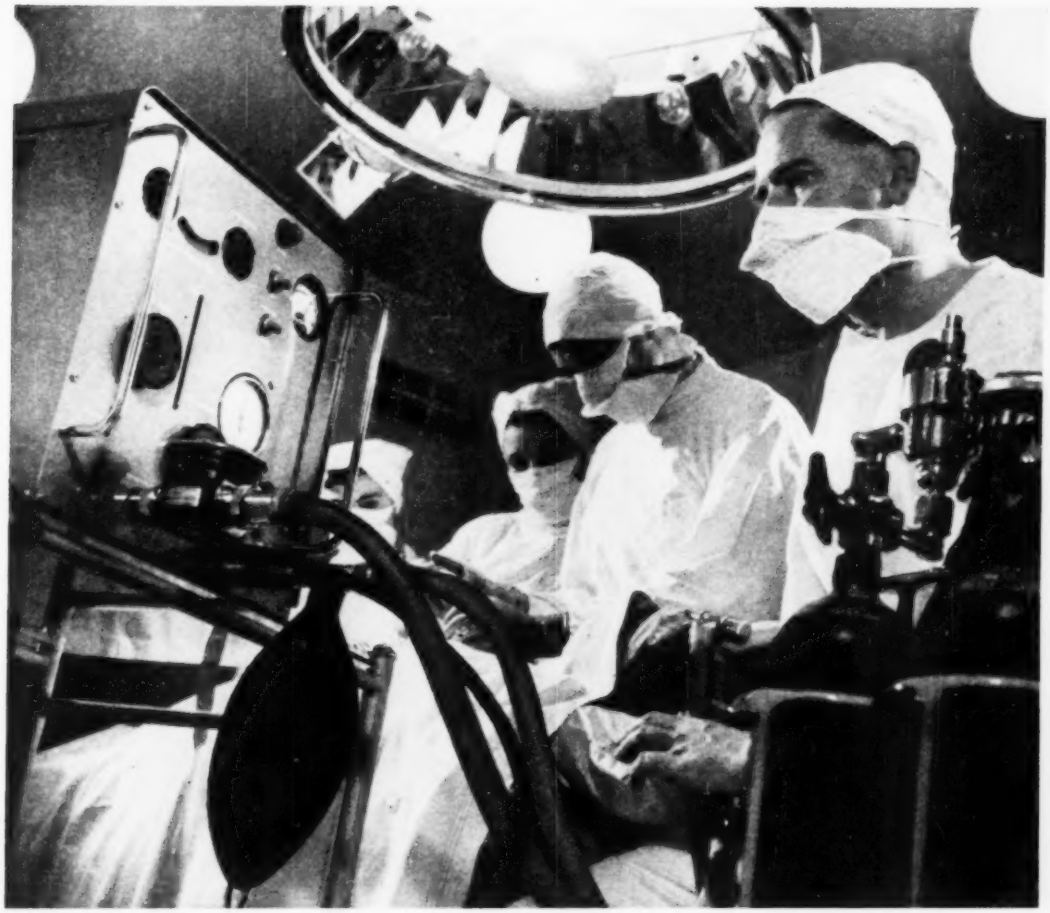

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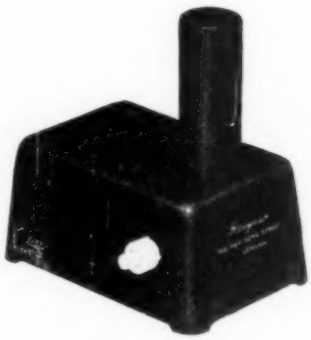

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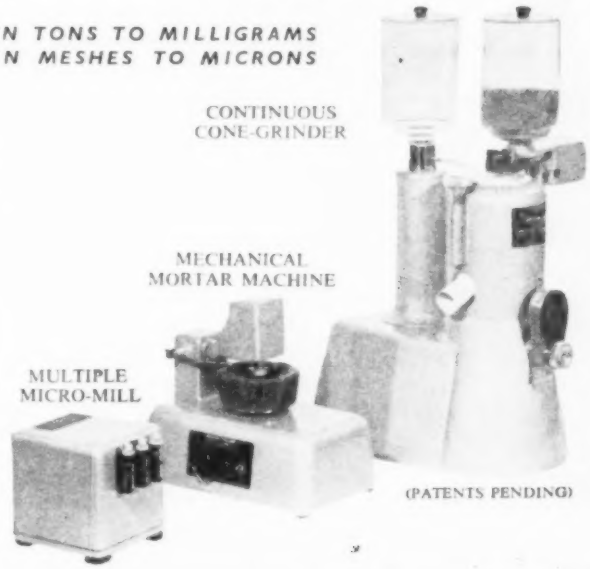

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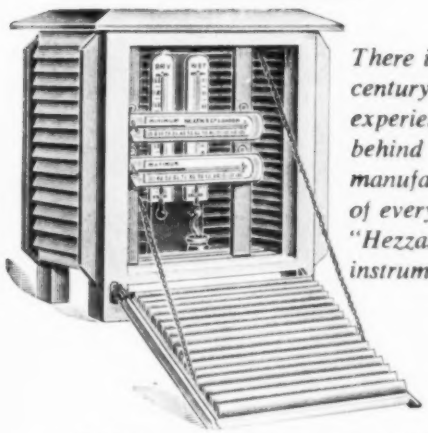

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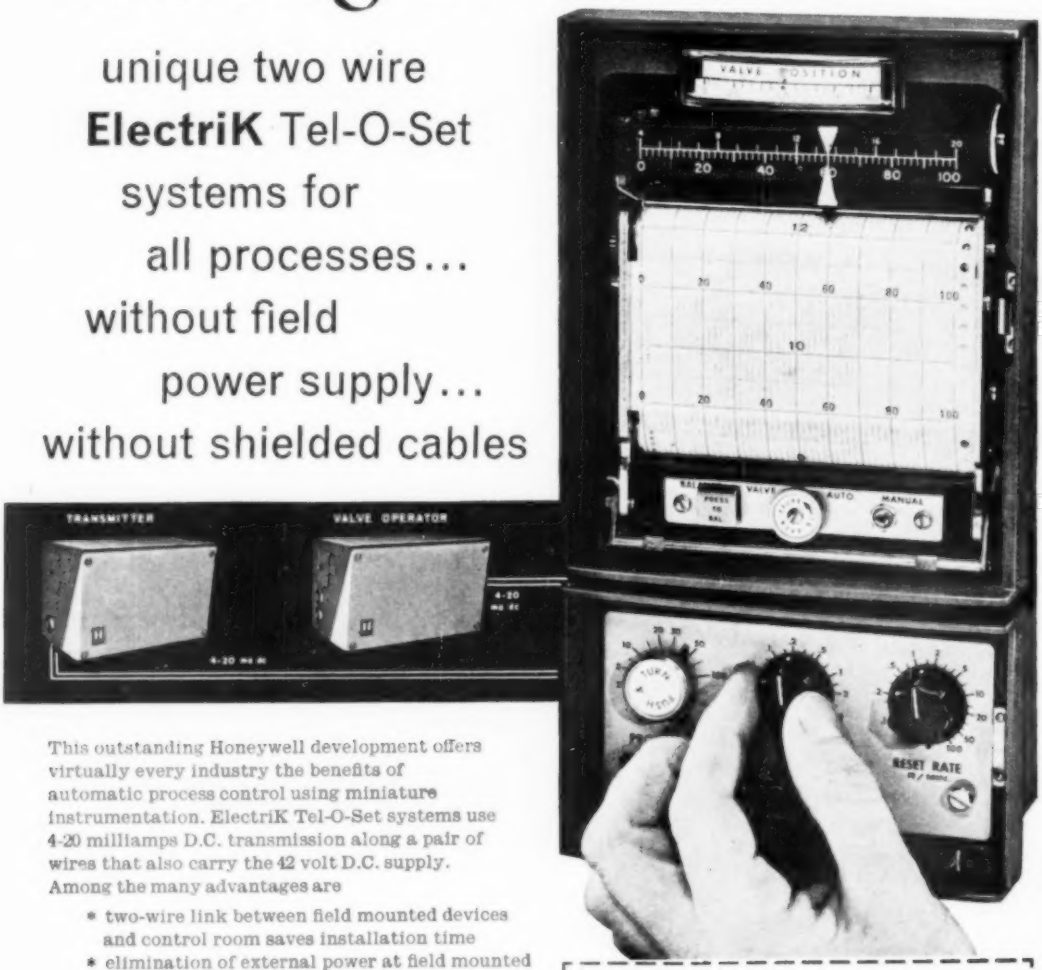

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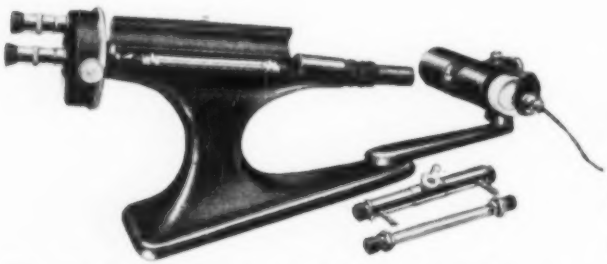

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PHYSICS IN GRAMMAR SCHOOLS

THE recommendations of the Physics Panel of the Science Masters' Association and the Association of Women Science Teachers for new physics syllabuses for grammar schools in Great Britain[1] have three main points of departure from the usual run of school-teaching at the present time. A good deal of material which, on reconsideration, did not appear really fundamental has been discarded. Twentieth-century physics, including some of the most recent developments, has been included both in the Ordinary Level and the Advanced Level recommendations for the General Certificate of Education examinations. There has also been a determined effort to trace the development of the basic concepts as they are understood to-day—matter and energy, particles and waves—and to present the subject to the pupil as a unified study that probes the interchanges and interactions of these concepts from various points of view. They are, as yet, only recommendations; it will take some time before they crystallize into examination syllabuses, and probably still longer for them to establish themselves firmly in the curriculum—assuming that both of these consequences ensue. The Associations are, of course, hopeful that this will happen. If it does not, the chances of establishing an effective system of science teaching, within the next twenty years, seem remote. The recommendations are a 'breakthrough' in the original sense of the term, which means starting an attacking movement by finding an opening in the opposing side's defence—after, in this case, a long spell of safety play on the blind side. This metaphor is appropriate here, because the most enterprising breakthrough will lead nowhere unless it is supported by the rest of the team. Now is the time for all progressive teachers to come to the aid of the Panel.

The opposing side in this case is the aggregate of all the well-known difficulties that beset the teaching of science in schools; the reasons for believing that they can be outflanked will be given shortly. In addition, it must be frankly stated, there is a certain distrust in some university quarters of the capacity of the schools to manage anything except teach pupils to pass examinations. Views that have been expressed in this sense cover the whole range from deploring the efficiency of school instruction that anticipates most of the first two years of a university course, to writing off as a total loss most of what has been inadequately done at school and having to start again from scratch. To the university lecturers who may well say that the suggested new syllabus is adding to the factual knowledge milling around unco-ordinated in the undergraduate mind, and that they would prefer, instead of a nodding acquaintance with nucleons, a clear capacity to distinguish between an ampere and a volt, one would counsel patience. The recommendations are on their side all the way. For the whole object is to present physics in the middle school as part of the general education of all pupils, in a way that can be grasped; and to continue with advanced work for the future specialist in the same spirit, concentrating on the matter that is fundamental and can be readily understood. As Mr. J. L. Lewis has pointed out[2], the great beauty about studying radioactivity experimentally is the immense scientific content that can be extracted with very simple mathematics; and this is the sort of bias that the new syllabus has. There is a good chance that pupils may be really educated while they are learning, as well as passing an examination at the end of the process.

A good chance: But is it the best chance? It has been said that, in aim, the recommendations are to some extent at variance with those of the Ministry of Education Pamphlet No. 38, which presents the study of science as a voyage of discovery[3]. Is the offering of facts and the establishment of modern concepts by lecture and film and sophisticated apparatus a substitute for simple first-hand investigation with primitive equipment? Of course it is not. When teachers are as familiar with the new subject-matter themselves as they are with those topics which experience has shown susceptible to fruitful discovery-voyages (and there is not as wide a repertoire of these as one might think), the right methods will be developed to fit the material. There is no necessary incompatibility; it can be the best chance if we make the best of it.

The first part of the recommendations, covering the basic five-year grammar school course to be taken by all pupils, deals with fundamental ideas of mass and motion and force, the properties of solids and fluids, mechanical energy and heat energy, light and vision, vibrations and waves, electrical energy, atomic structure, and nuclear energy. It omits much that is of purely mathematical interest, such as resolution of forces, kinematic equations, problems on the laws of motion, and work on the inverse-square law. The wisdom of these omissions at this stage is apparent when one considers (*a*) the difficulty they cause, and (*b*) the resulting pictures in the young mind when they are eventually mastered. Later, it will be easy and appropriate to explain

that there are convenient alternatives to the entirely general and sufficient principle of moments: that $x - t$ can be integrated; that Newton disclosed a little more than the magic formula $F = mf$; and that the inverse-square law is an essential geometrical property relating fields and particles in space, rather than something that works for sums that prove formulæ about magnets that must be learned as homework.

The second part, for the future scientist (and it must be remembered that very few people taking this sixth-form course will go on to do physics at the university, so that this is the general education of the scientist rather than the early specialization of the specialist), differs essentially from the present Advanced Level course chiefly in the emphasis given to vibrations and waves, to alternating current, and to modern physics, including such topics as the wave-particle duality of matter. But a good deal of purely memory work, and matter more appropriate to technology or applied mathematics, has been removed.

In an appendix, the essential ancillary mathematics has been tabulated, with the comment that this is what all scientists should be expected to master, and that it ought to be possible to cover it in two periods a week. It does not look too terrifying, and with the incentive to apply it to some really interesting physics it could be done.

Finally, it might be mentioned that the Associations have in active preparation (by their "Fourth Panel") sixth-form syllabuses for the general education of the non-scientist. Drafts are available for individuals who wish to see them for comment, but not for publication; and they have the same enthusiasm, the same sense of a pressing need, and the same realization of what can be achieved if it is seriously attempted.

We now come to the opposition. First, there is the admitted incapacity of very many physics teachers to branch out suddenly into new fields. The Panel says: "There are parts of the syllabus which some of us have never taught, and which we do not feel competent to teach. Universities and Technical Colleges are already arranging suitable short courses, and it is hoped that the Ministry of Education and local authorities will realize the importance of assisting in bringing teachers up to date". The widespread and regular running of such courses, starting immediately, would seem to be a first essential. It should be as much of a tradition for the science teacher to go back annually to the university as it is for the linguist to take his annual trip abroad, and all universities and places of higher education should participate in this. Next, there is the question of man-power available. The situation here is beginning to improve, and the new syllabuses should add appreciably to the attractiveness of school-teaching; the young graduate at present feels that he will never need to use his advanced knowledge in school work, and that it destines him for research. The realization that he will be extended, that he can still be a physicist as he understands the term, and that there are unlimited opportunities for research in the field of developing teaching methods and demonstrations, should attract a higher proportion of the best people. The co-operation of university physics departments in presenting this picture, which has always been valid to those who really understand what goes on in schools, could be offered with open eyes.

The matter of equipment would seem to require a combined operation. It would be easy, for a sum in the region of £500, to provide a nucleus of apparatus 'off the peg', which would enable a fair range of basic experiments to be done. It certainly exists, and some firms have specialized in apparatus for modern physics teaching. At the same time, many schoolmasters do not think along these lines, and prefer relatively simple home-made apparatus. Whichever way it is approached, the services of a technician will be not a luxury but a necessity: no such apparatus is 'school-proof', and maintenance and safety precautions in any laboratory equipped for proper teaching cannot be looked after by a full-time teacher. The alternative would be, of course, to use film, and film-strip, and film again . . . but teachers, who have taken the trouble to re-learn their subject in order to make it up to date and stimulating, are not going to be fobbed off with the cheap and easy way. For things such as counters and ionization chambers and gamma-ray sources there must, incidentally, be a good deal of equipment in Civil Defence stores that could easily and safely be passed over directly to schools; it seems to be almost a law of Nature that redundant apparatus must first pass to Government surplus dealers, where it stays because nobody can afford to buy it; but there must be some way of circumventing this in a good cause. The combined operation envisaged, however, is something at the highest level. The Ministry of Education, when it is decided whether these recommendations are desirable, should ask the Minister for Science to take over, and to arrange for the design and supply of suitable equipment. If it can be done for the training of Civil Defence wardens, it can be done for the education of the ordinary citizen.

It is difficult to forecast how the recommendations are going to work out in the matter of teaching time; though it is significant that several topics which lend themselves to a range of orthodox practical exercises, or to tedious mathematical proofs, have been omitted. It would appear that the syllabus has been lightened, particularly for the average sixth-former and for those who would at present be taking Ordinary Level physics as a separate subject. It remains, if the scheme is accepted, for the examining bodies and the teachers to interpret it in the spirit in which it has been framed.

[1] *Science and Education: Physics for Grammar Schools.* A Section of Part I of the Science and Education Report issued by the Science Masters' Association and the Association of Women Science Teachers. (Published for the Associations by John Murray, 1961.)

[2] "The Place of Atomic and Nuclear Physics in Modern Teaching", by J. L. Lewis. Paper delivered at a short course for science teachers at University College, London, April 1960.

[3] *Science in Secondary Schools.* Ministry of Education Pamphlet No. 38 (H.M.S.O., 1960).

PRELUDE TO SOCIOLOGY

Charles Booth

Social Scientist. By Prof. T. S. Simey and M. B. Simey. Pp. x + 282. (London: Oxford University Press, 1960.) 30s. net.

CHARLES BOOTH (1840–1916), a Liverpool merchant and shipowner, who in his spare time and without any institutional or financial assistance surveyed the life and labour of the entire population of working-class London at the end of the nineteenth century, was indeed a heroic figure. Prof. and Mrs. Simey, in their very readable account of his life and work, have made out a good case for thinking that his contribution to the establishment of sociology on an empirical basis has been much undervalued. The mere magnitude of his achievement still leaves one dazed. To survey every single street, every court and block of buildings in the metropolitan area; to check on the resources of every family; to catalogue and describe every industrial enterprise; and in the final survey of religious influences to visit every chapel, church and social agency; to do all this with a handful of collaborators and with no modern methods of data processing was an incredible achievement.

Booth's survey, *Life and Labour of the People of London* (3rd ed. 17 vols. 1902–3) was the pioneer social survey. Nothing quite like it had been carried out before. Within the limits which Booth set himself it gave a factual picture of London working-class life which was vivid, unsentimental, accurate and detailed. The volumes on poverty, which indicated with irrefutable evidence that more than one-third of London's population were at all times more or less in want, changed our social policies, and led ultimately to the introduction of the Welfare State.

This, perhaps, has been recognized by social historians. The Simeys, however, claim more. Booth was also, they hold, a great social scientist, one of the founders of empirical sociology, and it is this aspect of his work that has been unduly neglected. Sociology before Booth was largely deductive. Booth insisted on the need for facts. "The *a priori* reasoning of political economy", he said in a paper to the Royal Statistical Society, "fails from want of reality. At its base are a series of assumptions very imperfectly connected with the observed facts of life. We need to begin with a true picture of the modern industrial organism". In his collection of facts Booth relied on a combination of two things: statistics and first-hand observations. Accurate statistics were essential to get the picture in objective proportion; but alone they could mislead, and first-hand observation was needed to add colour and life. To this end Booth went endless walks to see for himself; lived in cheap lodgings; personally attended hundreds of religious services; and filled endless notebooks with his impressions and observations. There is no doubt an important lesson here, which in a day of more plentiful statistics may be overlooked. Booth, perhaps, had too many facts. He worked before the introduction of sampling methods, and his theoretical apparatus was not strong enough to enable him to make a meaningful selection. Sometimes from the mass of data important working hypotheses and conclusions emerged, which led to practical action, as in the case of old age pensions, for which Booth was largely responsible; at other times Booth ended up with detailed descriptions from which nothing very conclusive could be derived. Some of the ingredients of a true science of society were still lacking in Booth's work. But no science is possible without facts, and Booth demonstrated in a new way and on a new scale what facts meant in the study of society. The Simeys have made out their case. Booth must properly be regarded as one of the notable pioneers of empirical sociology.

L. S. HEARNSHAW

ELASTIC SHELLS

The Theory of Thin Shells

By V. V. Novozhilov. Translated by P. G. Lowe. Edited by Prof. J. R. M. Radok. Pp. xvi + 376. (Groningen: P. Noordhoff, Ltd., 1959.) 36 D. fl.; 9.50 dollars.

Proceedings of the Symposium on the Theory of Thin Elastic Shells

Delft, 24–28 August, 1959. Edited by W. T. Koiter. (International Union of Theoretical and Applied Mechanics.) Pp. ix + 496. (Amsterdam: North-Holland Publishing Company, 1960.) 55s.

THE theory of elastic thin shells has undergone considerable developments in the past few years, and it is good to see two excellent books on the subject, one concerned to present the elements of the theory to a beginner and the other to mark some of the bounds of our present knowledge.

In *The Theory of Thin Shells*, Prof. V. V. Novozhilov develops the linear theory of the stress and displacement of thin shells in terms of the familiar assumptions of the classical Love–Kirchhoff theory, that normals to the middle surface of the shell remain normal after the displacement, and that stresses on surfaces parallel to the middle surface are small. The relevant parts of the geometry of surfaces are developed *ab initio* in a simple and lucid manner, which should be well within the compass of any engineering undergraduate. With this foundation, Prof. Novozhilov is able to present the elastic equations for a general shell in the simplest practicable form, and so to save the reader the trouble of following a number of separate derivations of equations for special shells. In the succeeding development of the theory, special place is given to the method of complex components, which has not been discussed satisfactorily in previous books in English. The later chapters, on membrane theory, cylindrical shells and shells of revolution, contain most of the important standard solutions in these fields, including those for reinforced cylinders. Special mention should be made of the section on the toroidal shell, which brings out the inadequacy of the membrane theory as a first approximation in this problem, and gives results in a reasonably compact form.

In all, this book can be recommended with confidence as a first course on the subject, and should also prove valuable to experienced workers in the field. The translation is very easy to read, and the type-setting is excellent.

For workers carrying out research on the subject, the proceedings of the symposium on the theory of thin elastic shells will be both stimulating and informative. The subjects of the papers were deliber-

ately limited to problems involving either non-linear behaviour or two independent variables, and the volume has a unity of purpose not always found in a symposium. The papers range from a discussion of the basic approximations involved in a first-order theory of shells (W. T. Koiter) to solutions of particular problems of more immediate practical interest, like the "Bending at the Oblique End Section of a Cylindrical Shell" (A. van der Neut). A detailed discussion of the various papers is beyond the scope of this review, and would, in any event, reflect the tastes of the reviewer more than the importance of the contributions. Some of the work, for example, "On the Unsymmetrical Snapping of Shells of Revolution" (E. I. Grigolyuk) or the beautiful experimental results of W. Schell on the buckling of cylindrical shells, will probably become classical in the literature. Other papers, especially those on the general equations of equilibrium or motion, deal with issues which are still controversial, but pave the way for a more mature understanding of the whole subject at some later date.

The publishers are to be congratulated on the rapid and pleasing production of this volume, and the orgahizers of the symposium on bringing together so much useful work. J. W. CRAGGS

CELLULOSE PULP FROM WOOD

Pulp and Paper

Chemistry and Chemical Technology. By James P. Casey. Vol. 1: Pulping and Bleaching. Second edition, revised and enlarged. Pp. xix + 675. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1960.) 147*s*.

THE first edition of this work, published in 1952, has proved so valuable to the industry that there is really little need for the author to justify the present edition by stating in his preface that ideas are changing faster than practice. A measure of the rate at which this is occurring may, however, be obtained from the fact that Volume 1 of the first edition, which dealt with pulping and bleaching and paper-making, now becomes two volumes, of which the first is now under review. Thus, there are now approximately 450 pages on pulp and 120 pages on bleaching, as compared with 250 and 70 before, respectively.

The plan of the book follows the same general lines as previously, but naturally developments which have come to the fore in the past ten years receive due attention in their appropriate places. These include continuous pulping methods, chlorine dioxide bleaching, magnesium-base liquor recovery, the removal of bark from trees by chemical methods, hardwood pulping, and whole wood-fibre (particle board) manufacture. The portions of the book which deal with these are valuable summaries of our knowledge of these important subjects existing to date. Numerous literature references are provided throughout (nearly 1,280 in all).

A criticism levelled in review against the first edition was the almost exclusive American outlook, especially in the literature references and in the treatment of those fibres other than wood which are not commonly used in the United States. This still applies. Thus one might well infer that there have been no advances in the manufacture of esparto, rag and straw pulps, since the sections involved are almost unchanged. Indeed the word 'recent' is used as in the first edition to describe work carried out in 1948. The sections on esparto, bamboo and rag are so sketchy as to be of little or no use to those interested in them; this will apply to many readers outside the United States. Furthermore, the erroneous attribution of low recovery in the straw process to the presence of silica (also pointed out in review) recurs in this edition.

However, it is evident that the author is writing primarily for the American reader, and presumably, therefore, sins of omission cannot be held too strongly against him. As a presentation from the fundamental point of view of up-to-date knowledge on the pulping of wood the second edition of this work will undoubtedly command the same high status as its predecessor. JULIUS GRANT

HETEROMETRY

Heterometry

By Prof. Mordechai Bobtelsky. Pp. viii + 229. (Amsterdam: Elsevier Publishing Company; London: D. Van Nostrand Company, Ltd., 1960.) 42*s*.

THE heterometric method was introduced by the author, Prof. Mordechai Bobtelsky, of the University of Jerusalem, and the present monograph gives details of the varied and unique applications of this new technique in the fields of inorganic, physical and analytical chemistry. The heterometer was developed as an instrument for observing the instantaneous variations in optical density when a beam of light is passed vertically through a cylindrical absorption cell in which a heterogeneous reaction, for example, precipitation, is taking place. Colour interference is suppressed by placing suitable filters in the path of the light. Variations in the optical density are observed using a photometric cell, the solutions being stirred at a constant convenient rate. Since 1953, Prof. Bobtelsky and his co-workers have studied many thousands of reactions by means of this method. Heterometric titrations can give valuable information relating to the formation of primary or intermediate products during the formation of insoluble complexes, and can thus provide data which are unobtainable by ordinary turbidimetric measurements.

The combination of the heterometric method with the more classical applications of conductimetry and potentiometry are discussed for specific reaction systems. Considerable information is also provided indicating the quantitative analytical semi-micro applications of this new method, the determination of traces of a metal (0·1 per cent) being heterometrically possible even in the presence of more than 99·9 per cent of polyvalent foreign metals. Examples are extensively given of normal salt analyses and of the behaviour of many chelated metal ion–organic compound derivatives as recorded by heterometric analysis.

The final chapters of this monograph deal with the results of numerous researches on the formation of insoluble compounds in various solvents, for example, the metallic derivatives of aliphatic and

aromatic dicarboxylic acids, and of allied derivatives of the oxycarboxylic acids, polyphosphate complexes, thio derivatives, interaction of metal salt solutions with dyestuffs, the study of heterogeneous chain reactions and the question of inorganic-organic polymer formation are all topics which are discussed by reference to much graphically illustrated experimental data.

This is the most authoritative compendium of heterometric research investigations which has so far been published, and will, undoubtedly, prove of the greatest utility to the research worker studying heterogeneous phase systems, as well as to the analytical chemist and the university teacher. This is a modern technique which may have much future application, and it is pleasing to note that heterometry forms one of the subjects to be presented at the eighteenth International Congress of Pure and Applied Chemistry in Montreal next August.

D. T. Lewis

ARCHÆOLOGY IN ISRAEL

Hazor II

An Account of the Second Season of Excavations, 1956. By Yigael Yadin, Yohanan Aharoni, Ruth Amiran, Trude Dothan, Immanuel Dunayevsky and Jean Perrot. With a contribution by S. Angress. (The James A. de Rothschild Expedition at Hazor.) Pp. xxiv + 174 + 210 plates. (Jerusalem: Magnes Press of the Hebrew University; London: Oxford University Press, 1960.) 178*s.* 6*d.*

THANKS to the efforts of Dr. Yadin and his army of assistants, Hazor must be one of the most widely known of ancient Palestinian sites. Its importance lies not only in the outstanding interest of its excavated remains, but also in the fact that sufficient was known about the history of the city before the excavations ever began to enable these remains to be related to historical events, and to be dated accordingly with a fair degree of accuracy. In the second season of excavations work was concentrated in two areas on the *tell* proper, and two in the lower 'enclosure', which has now been proved conclusively to have been the site of the Canaanite town of the Middle and Late Bronze Ages, finally destroyed some time in the middle of the thirteenth century B.C. by (so Yadin thinks) the invading Israelites. In this lower city, the most important discovery has been that of a Canaanite shrine, with cultic objects (including a mask and a bronze standard) of outstanding importance for the history of Semitic art and religion, and also of other buildings which Dr. Yadin interprets (not very convincingly) as cultic. On the *tell* the chief buildings excavated were a fine pillared storeroom, attributed to Ahab; the Israelite citadel destroyed by Tiglath-pileser III of Assyria in 732 B.C.; and a casemated fortification wall probably built by Solomon. Individual objects from the *tell* included a beautiful marble incense ladle in the form of a hand, and several highly important Hebrew inscriptions. Space does not permit us to record here any more fully the discoveries of the archæologists. They are all now published lavishly, in this magnificent volume full of drawings, photographs and data, so that students in future will have no excuse for not knowing what has been found at Hazor.

They will, unfortunately, have far more excuse for not knowing exactly where it has all been found. In a review of the first volume of this report (*Nature*, 183, 951; 1959) I questioned the validity of the methods used by Dr. Yadin to unravel and interpret the complicated series of superimposed building remains at Hazor. The appearance of the present volume has, if anything, strengthened my belief that the analysis of the remains is not nearly as accurate and as detailed as it could be. This is the result both of a faulty method of excavation and of a faulty system of interpretation. The method is faulty because too much attention is paid to the levels of individual structures and surfaces, expressed in actual heights, and not enough to true stratigraphy. Where the floors are relatively and consistently level over a wide area, and the succession is regular, this may not matter too much; but such conditions are the exception rather than the rule. Where the ground slopes, and the ancient inhabitants have built on terraces, as they have in area *F*, for example, Dr. Yadin's method of excavation is fraught with danger. The confusion in area *F* is indeed great, and the reader (and, one suspects, the excavator) is quite at a loss to know which structures belong to stratum 1*A* and which to 1*B*. These uncertainties are, admittedly, openly acknowledged by the excavators, and Dr. Yadin is, no doubt, to be highly commended for allowing a member of his staff to publish a 'minority report' expressing serious differences of opinion, as M. Perrot does in a long footnote on p. 128ff.; but such differences of opinion do not inspire the reader with much confidence in the interpretation elsewhere.

This brings me to another point. For all the lavishness of illustration and documentation in this report, the record is still not full enough to allow the reader to form his own judgment about the meaning of the evidence presented. Prof. De Laet has well said (*Archæology and its Problems*, p. 52) that the test of a good excavation report is that the reader "ought to be in a position to reconstruct the whole excavation, almost every turn of the spade, in such a way that he can scrutinize most critically the conclusions reached by the author". The Hazor report fails this test. It is just as important that the reader should see for himself that one floor is higher or lower, and therefore later or earlier, than another, as it is that he should be given illustrations of the forms of Hebrew letters, to judge them for himself. The only way to illustrate stratigraphy is to publish accurately drawn and objective sections; and there is not one in this book. Without them, many of the fine plans are almost useless.

Finally, with regard to the faulty system of interpretation: does Dr. Yadin really want us to believe that all over his site the succession of superimposed floors and 'strata' is regular and orderly; that there was no local destruction and rebuilding; and that the structures under, for example, 'Stratum VI' always belong to 'Stratum VII'? Such is the general impression obtained from this report; though on p. 165 it is admitted that "certain layers in sub-areas which looked at first like real strata are in fact only local phases", while, in his footnote already mentioned, M. Perrot recognizes the presence, in area *F*, of "intermediate" strata, which, however, find no place in the neat synchronization table on p. 165. Such over-simplification is unrealistic, and detracts from the undoubted merits of the Israeli excavations at Hazor.

Peter J. Parr

THE ANATOMY OF MANAGEMENT

Exploration in Management
By Wilfred Brown. Pp. xxii + 326. (London: William Heinemann, Ltd., 1960.) 30s. net.

The Attitudes of Steelworkers to Technical Change
By Olive Banks. (Social Research Series.) Pp. viii + 152. (Liverpool: The University Press, 1960.) 25s. net.

THERE are few books that have been written by men who combine a wide experience of the practice of management with a developed system of ideas for the analysis of that experience. Mr. Chester Barnard's *The Functions of the Executive* was alone in eminence in this field until Mr. Brown wrote his latest book; but *Exploration in Management* will be as important in the study of organizations.

Mr. Brown's book has the sub-title *A description of the Glacier Metal Company's concept and method of organization and management*. This is most accurate, for the book is a report on the organizational relationships within that Company today and on the experience that has led to its structure. The book is in several parts, considering structure, policy formulation, communication, the organization of specialists and the sources of managerial authority. It gives us, in great detail, information about the problems that arise within an industrial hierarchy that adds much to our store of empirical knowledge.

Mr. Brown is primarily concerned with the problems of authority in organization; the clarification of superior-subordinate and collateral relations, and the attempt to reconcile the authoritarian concepts of mechanistic organization, writing with the wealth of understanding of human motivation in industry that stems from Elton Mayo, to which the Glacier Metal Company has contributed so much. This book is a part of the new trend in organizational theory in that it seeks a synthesis between these two ways of describing the social system of an organization, and Mr. Brown has developed specific mechanisms in the Company to limit and legitimate the use of authority. It is probably at this point that the book is weakest, for the concept of authority used is over-simplified and almost entirely defined in structural terms. Consequently, the compensatory mechanisms are also too simple and deceptively clear-cut. The Glacier Metal organization may, therefore, not be a generalized model applicable to all firms, or all similar firms, but it will be the stimulus to much new thinking in many.

Dr. Banks's book reports an extension of the previous work at the University of Liverpool on the social factors affecting technical change in a large steel works. She is concerned with an intensive analysis of the attitudes of steel workers to change, and her work is part of an international project. The European Productivity Agency has published a general report on the project "Steel Workers and Technical Progress" and the book under review represents the English contribution to this joint endeavour.

A questionnaire was administered to a sample of 278 men, all of whom had been affected by a major technical change some four years before the administration. The questionnaire was designed to elicit the attitudes of the workers to the specific changes they had experienced, in terms of wages, conditions, and social factors, and also to attitudes to change in general. The responses are analysed in terms of a naive socio-economic theory, but, although there is some valuable information in this study of perceptions of social change recollected in tranquillity, there is little that could be used as the basis for prediction. The data need to be re-worked in terms of more sophisticated concepts of social structure and industrial motivation before their full value can be realized. There are, scattered in the text, important references to the role of management in this successful change; but the questionnaire is not designed to put dimensions on this apparently crucial factor. This is regrettable, for we might have had more field evidence to consider against Mr. Brown's hypotheses.

F. J. Willett

TERRESTRIAL CRUSTACEANS

Isopodes Terrestres (Première Partie)
Par Prof. Albert Vandel. (Faune de France, Nr. 64.) Pp. ii + 416. (Paris: Éditions Paul Lechevalier, 1960.) 105 NF.

THE production of this valuable book could have been left in no better hands than those of Prof. Vandel, whose vast knowledge of the terrestrial Isopods represented by the sub-order Oniscoidea, has been collected into this comprehensive work.

The volume is divided into two sections: first an introduction, which contains facts of interest to the group as a whole, and secondly a systematic part dealing with some of the families of the Oniscoidea. In the first part the author outlines the history of the group, and then passes on to points of importance in the morphology of its members. These are dealt with under a number of headings: size, coloration, visual organs, integument (including ornamentation), sensory structures and cutaneous glands.

This is followed by an account of the segmentation of the body, the structure of appendages and sexual characters. A further section is concerned with geographical distribution and ecological factors and the origin and history of the Oniscid fauna of France. The first part ends with a survey of the principles of systematics and the classification of the Oniscoidea. The author points out that, of the twenty-one families, only members of thirteen, which are represented in the fauna of France, are considered in the systematic part. The latter begins with a key to determine these thirteen families, and it is unfortunate that in Section '*K*' of the key 'Armadillidae' occurs in error for 'Armadillidiidae', so that the former appears in both '*K*' and '*L*' sections.

The main body of the work represents a detailed account of the members of four of the families (Tylidae, Ligiidae, Trichoniscidae and Buddelundiellidae); the remaining nine families will be covered in the second volume. Each French species is dealt with under eight heads: synonyms, morphology, affinities, reproduction, parasites, ecology, geographical distribution, and palaeontology. Keys for the identification of genera and species are included wherever applicable.

The book is profusely illustrated with clear, well-labelled drawings, as well as a number of distributional maps; it will be indispensable to the specialist and invaluable to ecologists and students not only in France but also elsewhere.

E. M. Sheppard

Chemical Analysis of Cast Iron and Foundry Materials

By W. Westwood and A. Mayer. Second edition, revised by W. E. Clarke and H. Green. Pp. 586. (London: George Allen and Unwin, Ltd., 1960.) 63s. net.

THE analytical methods presented in this volume have been thoroughly tested in the laboratories of the British Cast-Iron Research Association. Fully detailed instructions are given in each case, and the practical details are accompanied by discussion of the relevant theory. In all cases, a general survey of existing methods is given, and the relative merits of alternative procedures are considered.

In this second edition the revising authors have modified or replaced a number of methods, according to experience and the results of analytical research. Such research has yielded an interesting new scheme for the analysis of cupola slag. A complete analysis of this material can now be carried out in less than one working day, with an accuracy comparable with that obtained by classical methods.

The short section dealing with laboratory practice and apparatus now includes a description of separations by solvent extraction procedures. Instrumental methods receiving brief attention are flame photometry, polarography, spectrography and X-ray fluorescence spectrography. A description of a particular absorptiometer has been replaced by a general account of the basis of absorption spectrophotometry and of spectrophotometric instruments—a particularly sensible modification to the text.

The methods given in this book are capable of wider application than the title suggests. The clarity with which the subject-matter is presented makes it possible for the analyst to assess the applicability of the individual methods to general inorganic analysis, as well as to the analysis of all classes of ferrous materials. F. L. SELFE

Theoretical Elasticity

By Carl E. Pearson. (Harvard Monographs on Applied Science, No. 6.) Pp. xi+218. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1959.) 48s. net.

THE writer of this book states that its purpose is in part to discuss modern methods in elastic theory, and in part to provide a compact summary of such methods.

The first four chapters contain a detailed account of vectors and Cartesian tensors, and of their use in describing infinitesimal strain and stress. Chapter 5 gives a summary of the basic equations of classical elasticity, and Chapter 6 a useful and interesting account of the general methods of solution associated with the names Somigliana, Betti, Kelvin, Boussinesq, Papkovitch-Neuber, Galerkin and Maxwell-Morera. Chapter 7 describes variational methods, though without illustration or application. Chapters 8 and 9 deal with topics in thermoelasticity and time-dependent problems, and Chapter 10 gives a brief introduction to non-linear elasticity.

The treatment is somewhat uneven; elementary topics are treated at considerable length and advanced topics sketched briefly. Some references are given, but not always enough to enable the reader to find proofs which have been omitted by the author.

J. F. BAKER

Physical Metallurgy of Stress Corrosion Fracture

Edited by Thor N. Rhodin. (Metallurgical Society Conferences, Vol. 4.) Pp. xiii+394. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959.) 98s.

AN engineer of great experience has recently stated that in no less than 27 per cent of all cases submitted to him for investigation the primary cause of the failures was ascribable to corrosion in one form or another, and in the majority of instances while the metal was under stress. The papers presented to the symposium recorded in this book give a very good account of the present state of knowledge regarding stress-corrosion and add to what is already known. In view of the important role of the crystal boundaries in leading to such trouble, it is, for example, valuable to have clear proof that the effect can occur even in single crystals. Since, if a solution of this extremely elusive problem is to be found, it can only arise from fundamental work, it is appropriate that more than half the book is devoted to the more theoretical aspects of the subject. Of the more immediately practical papers, although the stainless steels receive most attention, both mild steels and non-ferrous alloys are considered. This is an excellent account of the complex phenomena concerned with stress-corrosion failures and may be recommended unhesitatingly. F. C. THOMPSON

The Cathode Ray Tube Memory of the High Speed Electronic Computer of the U.S.S.R. Academy of Sciences

By V. N. Laut and L. A. Lyubovich. Translated from the Russian by Ruth Feinstein. Edited by F. A. Sowan. Pp. xi+90. (London and New York: Pergamon Press, 1960.) 35s. net.

THIS book describes the 1,024 word store used in the *B.E.S.M.* digital computer, which operates in parallel with a 39-bit word-length at a pulse-rate of 80 kc./s.

The first two chapters include a block diagram of the store organization, and a description of the storage tube, a barrier grid type using an aluminium back plate which stores 1,024 bits of data as a pattern of electric charges. Chapters 3 and 4 cover the writing and reading circuits used with the storage tube, and the balanced bridge circuit which isolates the reading and writing amplifiers. Chapter 5 describes the decoding of the address digits, the generation of the appropriate storage-tube deflexion voltages, and gives a discussion of the accuracy and stability of the spot position. Chapters 6–8 deal with the control unit, including test facilities, the coupling to the main computer, and the initial setting-up procedure. The final two chapters deal with the mechanical aspect of the store, and its performance in service.

Since the latest reference is dated 1955, the original text was presumably written in 1955 or 1956, and the type of storage described is generally considered obsolete. It has indeed been reported that the *B.E.S.M.* computer was equipped with magnetic-core storage in 1959 to replace the cathode-ray tube store. Thus, although the book gives a comprehensive account of the design and operation of the store, it should be regarded as a contribution to the literature of electrostatic storage tubes, rather than an account of present-day practice in digital computer engineering. J. C. CLULEY

FOUNDATIONS OF QUANTUM THEORY AND COMPLEMENTARITY

By Prof. L. ROSENFELD
NORDITA—Nordisk Institut for Teoretisk Atomfysik, Copenhagen

THE foundations of quantum mechanics were laid some thirty years ago. Thus, a whole generation has passed since these foundations were established, but for the new generation which is now coming up the situation is perhaps stranger still than it was for the physicists who had to struggle with those problems for the first time. The people who face a problem for the first time and have to think very hard to try to solve it have a more direct and lively impression of what is involved in the new ideas which bring about its solution. The next generation is presented with the finished work and often does not appreciate properly the difficulties that were involved in the solution of the problem. So it happened with relativity theory one generation after Einstein; some people started then to raise doubts about the very principles underlying the general theory of relativity. This episode is now forgotten; but we see the same phenomenon happening with quantum mechanics. Young physicists are raising doubts about the correctness of the basic ideas of quantum mechanics, and try to do it better. These efforts are, I am afraid, rather futile, because they rest on a complete misunderstanding of the problem, on a lack of appreciation of the really very difficult conceptual situation which quantum mechanics presents to us. This situation is not something that depends on any free choice, about which one might have this or that opinion. It is a problem which is imposed on us by Nature. After all, the existence of the quantum of action is a law of Nature; it is not something we have invented, but an aspect of Nature we have discovered. This discovery created, when it was made, a very embarrassing situation, and quantum mechanics is, in fact, the answer which physicists after many years of effort have been able to give to this challenge of Nature.

The discovery of the quantum of action was made in connexion with properties of electromagnetic radiation. In order to have something definite before us, we can therefore speak about the situation in the theory of light or electromagnetic radiation, although exactly the same can be said of electrons or any other constituent of matter. According to the classical theory of electromagnetism, light or any electromagnetic radiation can be described as a field, in the simplest case a field endowed with periodicity in space and time; the element of radiation is thus represented by a plane monochromatic wave, that is, a field distribution which has strict periodicity in space, with a certain wave-length, and in time a certain period connected with the wave-length and velocity of propagation by the wave equation. In order to have this strict periodicity, the field must be spread out over the whole of space, and it must persist during unlimited time; a pulse which only exists during a finite time does not have a sharply defined frequency, but a whole spectrum of frequencies; likewise, a limitation in space of the 'wave packet' implies a distribution of wave numbers (or inverse wave-lengths).

* Substance of a lecture given at the University of Tokyo on October 6, 1960.

Now, the discovery of the quantum implied that when radiation interacts with matter, as in the photo-effect or in the Compton effect, the amounts of energy and momentum exchanged in this interaction are not at all related to the distribution of energy and momentum in the radiation field, but are completely determined by the mechanical laws of conservation governing collisions between particles of definite energy and momentum; in this picture, a monochromatic radiation is represented by a light quantum or photon, behaving like a particle the energy and momentum of which are proportional to the frequency and wave number of the radiation. Thus, one was here led to describe radiation by means of another classical concept, which had hitherto been applied only to matter: the concept of the particle, which represents a concentration of energy and momentum at a single point of space and at any single instant of time. This is also, like the monochromatic wave, an ideal conception, and it is the extreme opposite of the latter; in fact, the two are mutually exclusive. Yet, they are intimately related by the equations:

$$E = h\nu, \qquad p = h\sigma \tag{1}$$

which express the proportionality between the energy and momentum E, p, concentrated in the particle, and the frequency and wave number ν, σ, defined by the plane wave.

These are at first sight very paradoxical equations: they relate together characteristics of the radiation which are contradictory to each other, and yet both are necessary to account for all phenomena (for the interference of waves is just as fundamental a phenomenon of radiation as the scattering of photons). The coefficient of proportionality, Planck's universal constant h, appears in the equations (1) as the product of two physical quantities—the energy of the photon and the period of the wave—which relate to two descriptions of radiation that are mutually exclusive. Thus such a situation demands more than just a mathematical analysis. The mathematics are extremely simple, but the question is to understand what these simple equations mean, as they seem to combine things that are mutually exclusive. What we meet with here is actually a problem of logic: What are we to do when we are confronted with such a situation, in which we have to use two concepts that are mutually exclusive, and yet both of them necessary for a complete description of the phenomena?

It is this logical problem which confers a very peculiar character on quantum mechanics. The situation was not quite the same with the relativity theory. Of course, in creating this theory, Einstein had also to make a very deep analysis of the fundamental concepts of space and time and of the relation between them, but although the result was quite revolutionary, he could perform this analysis within the framework of classical physics. Here we see that it is this framework itself that is too narrow logically: the task is to find a consistent way of using classical concepts so as to give well-defined meaning to mathematical relations like the equations (1) in spite of the fact that the parameters involved refer

to two contradictory images. The solution of this problem, to which a fundamental contribution was given especially by Heisenberg, received its final formulation from Niels Bohr; the new logical instrument which was created by Bohr is called complementarity. Complementarity denotes the logical relation, of quite a new type, between concepts which are mutually exclusive, and which therefore cannot be considered at the same time because that would lead to logical mistakes, but which nevertheless must both be used in order to give a complete description of the situation.

The idea underlying complementarity and making it possible to surmount the logical contradiction is, in fact, very simple. Contradiction arises when one tries to give a universal validity to the concepts that are mutually exclusive. If one tries to apply both of them to any situation irrespective of the circumstances of the situation, then, of course, one gets into contradictions. However, if one reflects on the use of all physical concepts, one soon realizes that any such concept can only be used within a limited domain of validity. These limitations may be disregarded so long as one is dealing with simple situations, as in classical physics: the constant h, which marks the limit of applicability of classical concepts, is so small compared with the actions involved in macroscopic experiments that we can ignore the limitation. Therefore the physicists of the nineteenth century had no need to think very deeply about this question. But after the discovery of the quantum of action has confronted us with such a situation, we are forced to analyse the logical relations between concepts, and to recognize their limitations. But once one has realized the simple fact that every physical concept is only defined with respect to a certain class of phenomena, to certain well-defined physical situations, it becomes easier to understand that different sets of concepts, although incompatible, may nevertheless be applicable to different physical situations.

Domains of validity of complementary concepts are not, in practice, rigidly exclusive of each other; they may overlap to some extent. Where they overlap, the concepts in question can both be applied, but of course not rigorously. A well-known example is that of a 'wave packet' of radiation. There can be no rigorously monochromatic wave: a real wave is always limited to a finite time-interval, Δt, and a finite region of space, the dimension in one direction of which we shall denote by Δx; such a wave can be analysed into monochromatic components with frequencies and wave numbers (in the direction x) distributed over intervals $\Delta\nu$, $\Delta\sigma_x$, the order of magnitude of which, according to the mathematics of Fourier expansions, is just $(\Delta t)^{-1}$, $(\Delta x)^{-1}$. We may regard such a wave packet as approximating the localization of the phenomenon in time and space with latitudes Δt, Δx, and at the same time, because of the relations (1), fixing the energy and momentum of the radiation within an accuracy $\Delta E = h\Delta\nu$, $\Delta p_x = h\Delta\sigma_x$. Thus, between the latitudes of the complementary pictures there is a reciprocity:

$$\Delta E \cdot \Delta t \approx h, \qquad \Delta p_x \cdot \Delta x \approx h \qquad (2)$$

which is an example of the famous 'uncertainty relations' holding for any pair of physical quantities complementary to each other.

This reciprocity illustrates a fundamental feature of the complementarity relationship. On one hand, there is no absolute limitation to the possibility of defining either of the complementary quantities: by making the wave packet infinite we obtain the idealization of a photon of well-defined energy and momentum; by making it infinitely small we have the ideal localization of the radiation at a single point of space–time. On the other hand, when we approach either of these extreme idealizations, we see that the complementary one becomes less and less defined, and is finally excluded: the fixation of the energy and momentum of the photon precludes its localization, and conversely, if we localize the radiation field, we lose the definition of the energy and momentum contained in it. Such reciprocal limitations correspond, of course, to real physical effects, and the complementarity relationship just expresses the fact that the experimental set-ups required for the determination and recording of each of the quantities in question are such as to impose on the complementary quantity the lack of definition expressed by a relation of the type (2). To realize quite clearly what is involved here, we must sharpen our language and ask ourselves, more searchingly than was necessary in classical physics, what we understand by a physical phenomenon. The precise definition of a phenomenon must include the description of the apparatus which defines the conditions of the experiment, and also some recording process (an index reading, a spot on a photographic plate, etc.) by which alone the phenomenon can be regarded as terminated: the physical quantities we are dealing with in our mathematical theories are in fact just such records of phenomena. Phenomena so defined can be in a complementarity relationship, and the accuracies of their recordings then stand in a reciprocal uncertainty relation.

Reciprocal uncertainty relations are in fact precisely what we must expect, from a purely logical point of view, if we are, as in quantum theory, in a situation in which contradictory pictures of the phenomena have to be resorted to for a complete account. In order to avoid trivial mistakes which would arise from an indiscriminate use of such contradictory concepts, we must have some way of delimiting their domains of validity, some prescription enabling us to decide in each case how far we can go with the help of each of them. The uncertainty relations tell us, so to speak, the price we have to pay for applying to the description of a phenomenon two sets of concepts which are strictly contradictory. It will be realized, without going into further detail, that the conception of complementarity means a very considerable extension of our way of speaking about Nature and about natural phenomena. It involves a new logical framework within which to arrange our concepts, compared with which the classical way of speaking appears very narrow because it is confined to the simple classical logic, governed by the principle of contradiction. Of course the classical logic remains the foundation of any argument we use, and certainly of our mathematics. But we find that when we deal with quantum phenomena it is too narrow: we must have a wider way of connecting together the various concepts, and this is provided by complementarity.

The most considerable change in our view of natural phenomena which is implied by this widening of our outlook is related to our conception of causality. In classical physics the expression of causality is the result of the mathematical properties of the equations expressing the laws of motion of particles and of propagation of the electromagnetic

field. When we are given the initial conditions, involving the initial values of the quantities and perhaps some of their derivatives, the solution of the equations is completely determined; and accordingly, the type of causality of classical physics is determinism. This is no longer the case when we have a complementary relationship, as is already suggested by the fact that we cannot then speak of all physical quantities with unlimited accuracy. One of the most obvious examples illustrating the new situation is the emission of the spectral lines: according to the quantum postulate, an atom in a high state of excitation can effect transitions to any one of the lower excited states; but there is nothing in the conditions of the phenomenon to tell us which of these possibilities will be realized in a definite case. Therefore, all we can do is to try to find the relative probabilities of their occurrence; it is just to cope with such situations that the concept of probability has been invented. The argument applies quite generally to all complementary situations; if we consider one set-up, in which, let us say, the field is localized within a certain space–time region, we have a probability distribution for all possible values of the energy and momentum, and conversely. These distributions are such that the corresponding average fluctuations are connected with the complementary time and space latitudes by reciprocity relations: if the field distribution is very narrow in time, it is very wide in energy, etc. In other words, the kind of causality that is implied by the existence of complementary relations between concepts is statistical causality.

As is known, statistical causality was introduced, historically, in dealing with the affairs of human societies or states, which are notoriously undetermined: that is the origin of the word 'statistics'. It was for the first time applied in physics in connexion with problems of atomic theory, though not those concerned with the individual properties of atoms; it was introduced in thermodynamics, that is, in the study of the properties of very large systems of atoms, and later also of systems composed of a very large number of monochromatic waves of radiation. This occurred in the second half of the nineteenth century, when, of course, nobody dreamt of the possibility of such queer things as complementarity. At that time the justification for introducing statistical causality was simply this. We aim at a complete description of a gas as a mechanical system of molecules; but this could only be obtained if we could know at a certain time the exact positions and velocities of all the molecules of the gas; then we could solve, at least in principle, the mechanical equations for the system, and deduce in a unique, deterministic way the state of the gas at any future, or past, time. However, this ideal aim is obviously unattainable, and therefore the best we can do is to speak of the states of the system in terms of probability, just as, in view of the impossibility of predicting the exact time of a man's death, we speak of the probability of his living for so many years.

The concept of probability was thus used with a sort of apology, in default of something better. This attitude was of course quite natural for people believing in determinism, believing that the Creator had imposed on Nature, once for all, rigid laws that had to be obeyed and were so contrived that they could only yield a single, predetermined, result. Unprejudiced observation of the world around us, however, will soon reveal that this idea of rigid determinism is a fiction, an unwarranted extrapolation from a very limited experience, and that there is no real justification for it. On the contrary, if we want to describe immediate experience, surely we must say that all our judgments about Nature or about ourselves are judgments of probability: we are never in a situation in which we know all the conditions for applying laws which would give us a unique answer. Thus, statistical causality appears in fact as more natural, more directly adapted to our actual needs than determinism; and it is much better to look at determinism as a limiting case of statistical causality, corresponding to statistical distributions very sharply peaked around the average values. From this point of view we are better prepared to accept the fact that the type of causality of quantum mechanics is fundamentally statistical; and we are even in a position to give exactly the limit of validity of classical determinism: the statistical deviations from classical behaviour become negligible in phenomena involving a large number of quanta of action.

Now, returning to the case of statistical thermodynamics, it is instructive to consider an objection to the point of view just outlined which is still often heard. It is all right to say that statistical mechanics is a self-contained theory, as I have tried to suggest; nevertheless it is conceivable that, if not human beings, at least imaginary beings, which Maxwell and his friends called demons, could be so small (and yet endowed with sense organs similar to ours) that they could observe the motions of the individual molecules of a gas; such beings could then give a deterministic description of it. I think the answer to this was already given very pointedly by Clausius, when Tait tried to use this fiction of the Maxwell demon to question the universal validity of the second law of thermodynamics by pointing out that those demons could bring about situations contradictory to the second law. Clausius's answer was: "We are not concerned with what demons can do, but with what heat can do by itself", which clearly means: with the phenomenon of heat which we can observe. I think there is a very deep truth in that answer, deeper perhaps than Clausius himself could realize at the time.

In fact, what the situation in quantum mechanics has helped us to realize is that science is primarily concerned with the communication of experience about phenomena, in other words, with statements made by human beings, and which other human beings are able to understand. For this very reason all such statements must make use of the concepts of classical physics, because classical physics is just the language describing the results of direct observation, the phenomena which we can observe with our senses, either directly or with instruments to increase the sensitivity, in any event, with recording systems composed of many atoms. If, then, we talk in this language about atoms which do not follow the laws of classical physics, we meet with the limitations of its use expressed by relations of complementarity. We thus see that this complementarity has its source just in the peculiar situation in which we find ourselves, as macroscopic systems, trying to describe the possible macroscopic interactions of our apparatus with the smallest elements of which Nature consists.

Now, if we look back at thermodynamics from this point of view, we see that it presents a logical problem which is just the same as that of quantum mechanics. Here also we are trying to describe

atomic structures in terms of macroscopic concepts, and we may do this in two different ways; we may be able to give a more or less detailed dynamical description of the atomic system, in terms of the motions of its parts; or we may describe its state in terms of the macroscopic quantities, such as volume, pressure, temperature, entropy, which are related by the laws of thermodynamics. Between these two modes of description there is a relation of complementarity; this is very clear if we consider the temperature and the energy, representing the thermodynamical and the dynamical points of view respectively. These two quantities are complementary to each other in the sense that if a system has to have a well-defined energy, it must be thermally isolated, and we cannot then ascribe to it any temperature, because in order to define the temperature we must establish thermal contact between the system and another, very large system, serving as a thermostat; conversely, if the temperature of the system is defined in this way, it exchanges energy with the thermostat, which means that its energy is not determined; in fact, we know that in this case this energy has a definite statistical distribution, the canonical one, the modulus of which is proportional to the temperature of the system.

This complementarity we can formulate in a more general and precise way, in wide-going analogy with the case of quantum mechanics, by setting up reciprocal relations between the statistical fluctuations affecting macroscopic quantities. Of course, the reciprocal limitation of the dynamical and thermodynamical modes of description has nothing to do with the quantum of action: the similarity of the two cases is on the logical level only; physically, they are completely independent of each other.

The fluctuations we are here considering are those which affect the macroscopic parameters defining the state of a system which is a small part of a larger, but finite, system; then, even intensive quantities, like the temperature, will exhibit fluctuations, for they are only exactly defined for infinite systems. It is easy to see that one must expect reciprocal relations between fluctuations of extensive and intensive quantities, that is, those quantities which (for a homogeneous system) are proportional to the number N of constituent elements of the system, and those which are independent of N. In fact, the fluctuation of an extensive quantity, the energy, for example, is proportional to $N^{1/2}$, while that of an intensive quantity, the temperature, say, is inversely proportional to $N^{1/2}$; the product of the two is therefore independent of N and cannot be made arbitrarily small by a change of the number of degrees of freedom of the system. A more detailed calculation shows that the products in question are of the form kC, where C is a quantity independent of the size, but depending on the physical properties of the system considered, and k is Boltzmann's universal constant. Thus, it is this constant which here plays a part analogous to that of Planck's constant in quantum theory: it is inversely proportional to Avogadro's number, which is thus seen to define a critical size of the system, for which the complementarity between dynamical and thermodynamical description becomes important.

This consideration is not as artificial as it may seem: it is easy to give examples of systems of this critical size, which can be considered from both the dynamical and the thermodynamical points of view. If we take as the systems under investigation droplets of emulsion distributed under gravity in a solution, we have a case in which the systems are large enough for us to see them and to follow their motion, which is a Brownian motion, and yet small enough for us to speak of their statistical distribution in the solution. As a representative thermodynamical quantity we may take the entropy S, which will fluctuate on account of this statistical distribution of the droplets. Now we need an intensive quantity characteristic of the individual motions of the droplets; for this let us choose the velocity v, which is subject to the well-known Brownian fluctuations due to the collisions with the molecules of the solution. A simple calculation gives in this case for the product of the two fluctuations:

$$\Delta S . \Delta v = k v_0$$

where v_0 is a quantity of the order of the mean atomic velocities inside the droplet. We see that the pattern of complementarity applies to the present case in all details just as in quantum mechanics.

So far, therefore, we have found that the atomistic view of the world involves in its description two stages of complementarity. The first and most fundamental one occurs in the account of the properties of individual atomic systems, the second when we want to describe the behaviour of systems of large numbers of atoms. In the first case, a relation of complementarity exists between two sets of concepts which were used indiscriminately in classical theory: the space–time localization and the energy–momentum balance; it becomes significant when the mechanical action in the process considered is of the order of Planck's constant. At the second stage, we have complementarity between the dynamical and the thermodynamical behaviour of large systems, the critical size being given by Avogadro's number. In both cases, as we have seen, complementarity essentially implies a specific kind of statistical causality.

Let us now venture for a moment into the field of biology. We here meet with a very peculiar situation: what characterizes the biological behaviour, in contrast with the behaviour of inanimate matter, is the existence of a certain structural order, either definite spatial structures such as those of the protein molecules, or more formal, topological structures such as the interconnexions of nerve cells in the brain. In any event, we notice the appearance of some kind of order which has a remarkable stability, and which can be reproduced. Now, the great event of the past few years has been the discovery, at the very lowest stage at which the phenomena of life appear, of possible mechanisms by which the maintenance and perpetuation of such a type of order can be understood in simple terms of physics. There is certainly no reason to expect that, with the most elementary, also the most elaborate forms of biological behaviour will not eventually be reduced, in a certain sense, to the laws of physics and chemistry, that is, in the last instance, to quantum mechanics, since according to the famous saying of Dirac quantum mechanics explains a large part of physics and the whole of chemistry. Now we may perhaps add: the whole of biology.

Yet this is not the whole story. It is quite obvious that, when we are presented with such complicated structural problems, it is practically impossible, even with the most perfect knowledge of all the laws of physics and chemistry, to predict what kind of organism will result from a given structure of such

complexity. We are here in the same situation as somebody who would know all about mechanics and is presented with a blueprint of some machine which he has never seen and which he does not know. It would be very hard for this person to guess the function of the machine, to understand why this particular combination of motions has been set up. We must realize that in order to get complete understanding of organisms we need the concept of function. We must somehow know beforehand what the function of a certain organ is in order to be able to understand its structure. We here meet with another type of causality, functional causality, which is obviously complementary to the ordinary causality of physics and chemistry, from which this concept of function is absent. Thus, we see that at the biological level we have another stage of complementarity, which again presents the same characteristics of mutual exclusiveness as the previous ones: on one hand, we have the complete description of organs in terms of physics and chemistry, on the other the functional mode of description, which will always be necessary for a complete account of such complicated arrangements of molecules as living beings. This complementarity is concerned with another aspect of atomic systems than just the size, although the size is rather critical, inasmuch as biological structures can only occur at a definite stage of molecular complexity, allowing on one hand for the necessary stability and on the other for the possibility of reproduction; but the main point here is the type of spatial ordering of the constituent atoms, which distinguishes biological systems from inanimate ones.

At this point I may perhaps be allowed to venture a little further still on the path of speculation, and raise the following question. The whole point of the logic of complementarity, in its application to the atomistic description of the world, is that the mutual limitations in the use of the classical concepts it implies, at each of the three stages we have recognized, are related in the last resort to the size of the sense organs of human beings. To be sure, there is no direct reference in physics or even in molecular biology to the human observer as such, but only to registering appliances which are entirely controllable physical systems. Still, the size of these appliances is dictated by the requirement that the complementary limitations be negligible in the account of their behaviour, and this effectively brings them to macroscopic size, that is, to a size adapted to our sense organs. There was a Greek philosopher, the sophist Protagoras, who used to say that "man is the measure of all things". There is a deeper truth in this than he could possibly fathom. This brings us to the question: Is the recourse to complementarity logic so to speak an accident, another of the many imperfections of human nature, and is it not conceivable that other rational beings, some kind of Maxwellian demons, could develop a different mode of description of Nature not affected by any complementary limitations?

The tentative answer I should like to submit is that there is nothing more accidental in the emergence of complementarity logic than in the emergence of man himself as a product of organic evolution. My point is that the concept of a thinking Maxwellian demon is self-contradictory. I suspect that the development of a computing and communication system like our brain demands about that complexity of organization which has been reached by our own species in the course of evolution. After all, it is an empirical fact that rational thinking has only arisen at the stage of mankind, presumably because it was only at this stage that a brain developed with a sufficient number of interconnexions between nerve cells to make possible this very peculiar behaviour which we call rational thinking. Hence the suggestion that no animal other than man or some being of equivalent complexity can possibly have any physics; and this degree of complexity, as we have seen, necessarily implies the introduction of complementarity in physical theory.

The view of physics, and in fact of science, which results from the development of quantum theory is very different from the scientific ideal of the nineteenth century; but it is by no means, or so it seems to me, inferior to it. The ideal for which such people as Huxley and Tyndall fought, the supremacy of human reason over all forms of irrationality, was based on the deterministic view of a Nature governed by inflexible laws, which the task of science was to discover and to formulate. These laws, by their very nature, would have absolute validity, and they would give a picture of the universe, in the literal sense of the word, a picture which could be contemplated, but from which the spectator, the human spectator, would be excluded, or at least reduced himself to an object of contemplation. The present conception, on the contrary, stresses the fact that at every stage the human observer intervenes in a very fundamental way by determining the very language in which the laws of Nature are formulated. The significance of the laws of Nature, from this point of view, is not that of drawing a picture of the world independent of who is looking at it, but rather of giving an analysis of the interaction between ourselves and the external world. At first sight it would seem that one thus introduces in science a subjective element. But the fear that the objectivity and rationality of the old view would be abandoned is entirely unfounded. True objectivity is simply the possibility of guaranteeing that the account of the phenomena will convey equivalent information to all observers, that it will consist of statements intelligible to all human beings. This objectivity is indeed ensured in quantum theory by the existence of transformations which allow you to pass at will from the point of view of one observer to that of another, who makes some other type of experiment. It is just the invariance of the laws of physics for such transformations that guarantees their objectivity, and nothing is changed in this respect by the advent of quantum theory.

Far from marking a retreat of human reason from the ambitious aim of the great pioneers of the preceding centuries, the new ideal of science appears as a tremendous advance towards this very aim. Compared with the old one, it is much broader of scope, much richer of content. It is more truly adapted to the actual situation that scientists have to face in their quest; the logic of complementarity enables us to cope with the dilemmas which this situation presents to us, and which were insoluble from the old point of view. I may therefore conclude on an optimistic note by assuring the younger generation that the instrument of rational analysis we are handing over to them contributes to a further increase of our power of understanding our position in Nature and of coping with the problems which it raises.

COMETS AND THE FORMATION OF BIOCHEMICAL COMPOUNDS ON THE PRIMITIVE EARTH

By Prof. J. ORÓ

Chemistry Department, University of Houston, Houston, Texas

INTERACTIONS of comets with the Earth or the Moon have been suggested by Urey[1], Fensenkov[2] and more recently by Whipple[3] in order to explain several terrestrial phenomena. It is estimated that about 40 million comets are now present in the solar system[4], and it has been calculated that about 100 comets have collided with the Earth since the formation of our planet some 5×10^9 years ago. (The value of 100 comets is obtained from Urey's comet-Earth collisional probability assuming a constant rate of comet formation. This value would be larger if the number of comets when the solar system was formed were several thousand times greater than at present[4].)

I suggest that one of the important consequences of the interactions of comets with the Earth would be the accumulation on our planet of relatively large amounts of carbon compounds which are known to be transformed spontaneously into amino-acids, purines and other biochemical compounds.

First, the amount of cometary matter (made mostly of carbon compounds) trapped by the Earth during its first 2×10^9 years can be calculated to range from 2×10^8 to 1×10^{12} tons on the basis of Urey's collisional probability[1] and the estimates of 1–10 km. for the diameter, and 0·01–0·05 gm. cm.$^{-3}$ for the density of the nuclei of comets[1,5]. The assumptions made here are that most of the cometary matter, neutral or ionized, was retained by the gravitational and magnetic fields of the Earth, and that the Earth's environment during the first 2×10^9 years was essentially reducing[6] and perhaps abiotic[7,8]. It is further considered that the high temperatures developed as a result of the collision impact would not essentially have altered the potential reactivity of the chemical species present in comets, since spectroscopical observations of pre- and post-perihelion emission[5], and chemical experimentation[9–11], attest to the thermal stability of the cometary carbon compounds. The high pressures developed on impact would, if anything, tend to condense the monocarbon species into linear chains of 2–6 carbon atoms[12].

Secondly, if terrestrial accretion of cometary matter from comets passing sufficiently close to our planet is considered, the amount of carbon compounds trapped by the Earth would be even larger. It is possible that this second mechanism of mass transfer which would result in a more continuous accretion of cometary matter was as important as the one by direct collision. Analogous mechanisms to those above have been offered for the terrestrial capture of non-volatile meteoric matter[3,8,13–15].

Thirdly, it is known from work on cometary spectra carried out for more than half a century and compiled by Swings and Haser[5] that comets contain large amounts of hydrogen, carbon, nitrogen and oxygen compounds, as indicated by the fluorescence emission bands of diatomic and triatomic radicals or molecules such as CN, CH, CH_2, C_2, C_3, NH, NH_2 and OH, and ions such as CH^+, OH^+, CO^+, N_2^+ and CO_2^+, observed in the heads or in the tails of comets when these bodies are at distances of less than 3 A.U. from the Sun. The CN band is generally the first molecular emission to appear on the tails of comets during the travel of these bodies toward the Sun, and it is also the band with the largest degree of extension into the comets' heads, followed in intensity by the C_2 and the C_3 bands. It is possible that the nuclei of the heads of comets contain frozen free radicals which are volatilized by radiant heat from the Sun[16,17], and it is also possible that they contain frozen ordinary molecules which are vapourized and photodissociated into radicals by the solar radiation[5,18]. These two points of view do not necessarily exclude each other, since it has been found recently that the NH radical can coexist with reactive carbon compounds[19]. In general, it is considered that the parent molecules of CN, NH_2 and OH are hydrogen cyanide or cyanogen, ammonia and water, respectively[5,18].

On the basis of the above considerations, it would be of interest to find out by experiment the products formed from chemical mixtures approaching cometary composition. This has partially been done by studying the products formed in reaction mixtures containing hydrogen cyanide, ammonia and water. Recent studies in my laboratory have provided evidence for the synthesis of adenine[20,21], 4-aminoimidazole-5-carboxamide, 4-aminoimidazole-5-carboxamidine and formamidine[22], and glycinamide, glycine, alanine and other amino-acids[23] from the reaction of hydrogen cyanide in aqueous ammonia. All these compounds and other unidentified products were formed more or less simultaneously in the same reaction mixture in a spontaneous manner. More than fifteen experiments have been carried out to the present time using concentrations of hydrogen cyanide of 1 to about 11 *M* and temperatures of 30–100° C. The synthesis of adenine, imidazoles, amino-acids and the other compounds has been demonstrated every time that the reaction product has been analysed for them.

In addition to hydrogen cyanide, ammonia and water, other reactive molecules such as formaldehyde, acetaldehyde, hydroxylamine and hydrazine could be expected to be formed by intercombination of cometary radicals. Experiments carried out with aqueous solutions of these compounds have also resulted in the formation of biochemical products. Thus, formaldehyde and hydroxylamine or hydrazine have yielded amino-acids, amino-acid amides and aliphatic acids[24–26]. Formaldehyde in the presence of calcium oxide is known to yield C_3 to C_6 monosaccharides[27]. Recently the synthesis of deoxyribose from formaldehyde and acetaldehyde has been observed for the first time in my laboratory[28].

Since glycine and glycinamide were two of the most frequent products obtained in the above amino-acid

synthesis, the polymerization of these compounds in aqueous ammonia systems was also studied. They were both found to give polypeptides which were characterized as polyglycines I and II by the infra-red spectra and chemical properties[29,30]. It may be added here that the synthesis of pyrimidines, such as uracil and cytosine, should also be possible by reaction of urea with certain C_3 compounds resulting from the symmetrical C_3 species of comets.

The mechanisms of synthesis of most of the above compounds have been elucidated, and in general follow lines in common with known chemical and biochemical syntheses. They have been briefly reported[31,32], and they will be published in detail elsewhere.

From the foregoing it appears reasonable that a large number of compounds of biochemical significance such as amino-acids, polypeptides, purines, pyrimidines, imidazoles and the pentoses, ribose and deoxyribose could have been formed from cometary matter trapped by the primitive Earth.

The present hypothesis of cometary origin of biochemical compounds on the primitive Earth is not to be considered as an alternative hypothesis to that formulated by Oparin[34], Urey[35] and Miller and Urey[36] and others, but rather as a complementary one since in both cases essentially reducing conditions for the primitive Earth's environment are assumed. This assumption of reducing conditions, or at least non-oxidizing, is borne out by geochemical evidence[5].

It can thus be visualized that after the Earth was condensed to approximately its present volume, having lost practically all the gases of the proto-planet's atmosphere[37–40], collisional and non-collisional mass transfer from the comets resulted in the accumulation on the Earth of significant amounts of reactive carbon compounds, which were mixed with similar, but perhaps less-reactive, compounds of magmatic origin[41,42], forming the early atmosphere and hydrosphere where organo-geochemical syntheses took place.

An important feature of this hypothesis is that it gives a plausible mechanism for the partial replenishment of the Earth's atmosphere by the continued accretion of gaseous compounds on the planet after all the Earth's original gases had escaped.

A second feature is that cometary collisions would lead to the concentration of relatively large amounts of carbon compounds in isolated regions of the primitive planet, making it irrelevant to the central biopoietic problem the extent of replenishment of the Earth's atmosphere. It need only be realized that a single comet would be equivalent to more than one million tons of organic matter, and that the effective concentration in the vicinity of the impact area would presumably be quite large due to the limited dilution caused by the small amount of water thought to be present on the primitive Earth[41,42].

A third, and perhaps most important feature, is that the reactivity of the chemical species present in comets and trapped by the Earth would be such that, under the increased gravitational field, and the other physical conditions developed on capture, they would be rapidly transformed into organic and biochemical compounds without the need of additional sources of energy; making the synthesis possible even if the energy input from electrical discharges, ultra-violet light, ionizing radiation and magmatic processes were limited.

As a final thought it is interesting to note that the predominant elementary composition of comets, and for that matter that of the Universe as a whole if we exclude the inert gases[43], is precisely identical to the elementary composition of proteins, that is, hydrogen, carbon, nitrogen and oxygen. The corollary is that given appropriate planetary conditions[44], the phenomenon of biopoiesis should be a probable event in our universe rather than a very improbable one.

In order to formulate more precisely the quantitative aspects of this hypothesis it will be necessary to carry out more detailed work on the statistics of the cometary population of the solar system, on the chemical composition of comets, and on the nature of the dust cloud about the Earth.

I wish to thank Drs. L. F. Biermann, G. H. Herbig, H. C. Urey and F. L. Whipple for valuable information.

The experimental work on the synthesis of biochemical compounds reported here has been supported in part by grant *G*-13117 of the National Science Foundation.

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OBITUARIES

Lord Stopford, K.B.E., F.R.S.

JOHN SEBASTIAN BACH STOPFORD was born near Wigan on June 25, 1888, and died on March 6, 1961, at Arnside, Westmorland.

He was educated at Liverpool College, Manchester Grammar School and the University of Manchester, graduating M.B., Ch.B. with honours in 1911, after gaining several distinctions and prizes during his medical course. After serving as a house surgeon at Rochdale Infirmary and assistant medical officer at Manchester Royal Infirmary, he became, in 1912, a demonstrator in anatomy in the University of Manchester. He was promoted lecturer in 1915 and in the same year he received the degree of M.D. with a Gold Medal for a thesis of outstanding merit on "The Arteries of the Pons and Medulla". He succeeded to the Manchester chair of anatomy in 1919 on the resignation of Prof. (later Sir) Grafton Elliot Smith, and in December 1934 he was appointed vice-chancellor in succession to Sir Walter Moberly. He combined his duties as vice-chancellor and professor of anatomy until 1938, when he resigned his chair and was appointed to a personal chair of experimental neurology.

His ability as a scientist was recognized by his election to the fellowship of the Royal Society in 1927, and he was the first Manchester medical graduate to achieve this high honour. Under the inspiration of Elliot Smith, his research work was predominantly neurological, and he collaborated successfully with his surgical colleagues (Sir Harry Platt, Sir Geoffrey Jefferson and Profs. E. D. Telford and John Morley) in the elucidation of various problems. His work can be divided roughly into three phases—his investigations on the blood supply of the brain, his anatomical and clinical studies on sensation, based mainly on the observation of many patients with peripheral nerve injuries, and his researches on the structure and function of various parts of the autonomic nervous system. He published more than sixty papers and an important monograph on "Sensation and the Sensory Pathways" (1930), besides contributing sections to several anatomical text-books. As vice-chancellor he was unable to indulge his flair for correlating basic and clinical research, but had he continued as a scientist he would undoubtedly have enhanced his already high reputation.

In a short notice one cannot even mention all that Stopford did for education and his University; but he was the best vice-chancellor Manchester has ever had and according to Sir Hector Hetherington (1956) "the best of us all" (the "all" refers to the members of the Committee of Vice-Chancellors and Principals). His worth was recognized nationally by his appointment as chairman, vice-chairman or member of such influential bodies as the General Medical Council and the University Grants Committee, the Commonwealth Fund, the Nuffield Foundation, the Interdepartmental Committee on Medical Schools, the Universities Bureau of the British Empire and the Council of the Royal College of Physicians, while locally he served as chairman of the Manchester Regional Hospital Board (1948–53), of the John Rylands Library, of the Royal College of Music, and on many other bodies. He was awarded honorary degrees by the Universities of Dublin, Leeds, Cambridge, Liverpool, Durham and Manchester, and honorary fellowships by the Royal College of Physicians and Royal College of Surgeons. He was knighted in 1941, created a K.B.E. in 1955, and he was included in the first list of life peers (1958).

He was a fine and imaginative teacher who helped to rescue anatomy from the topographical morass into which it had fallen, and who did much to close the gap which had developed between the basic medical sciences and clinical practice. He was a pioneer in the use of radiological methods in teaching living anatomy, and he was the first to take over from physiology the full responsibility for teaching histology. Both as a professor and vice-chancellor his sympathy with students and their problems was evident; and he was appreciated as highly by his colleagues in the Arts and other Faculties as by those in his own profession. His familiarity with education and research in all their manifold aspects was utilized, as the abbreviated list of his appointments given above indicates, by many Government and other bodies; and he was the chief inspiration for many of the far-sighted reforms in medical education recommended in the Goodenough Report.

He married Lily Allan, another Manchester medical honours graduate, in 1916, and they had one son. Theirs is the greatest loss; but those who served under him honour the memory of a distinguished scientist and supreme administrator and marvel that one who had gained so many honours could yet remain so human, humble and kind.

G. A. G. MITCHELL

Miss Ethel F. Bellamy

THE death of Ethel F. Bellamy on December 7 at the age of seventy-eight removes one of the last of those self-trained and dedicated workers who have done so much for astronomy and seismology in Great Britain. Miss Bellamy went to the Oxford University Observatory in 1899 as a personal assistant to her uncle, the late F. A. Bellamy, and was able to relieve him of some part of the work in the preparation of the Oxford zones of the *Astrographic Catalogue*. On the completion of these zones and under the direction of Prof. H. H. Turner, Miss Bellamy then undertook the reduction of the measures for the Vatican zones, work for which she was awarded a commemorative silver medal by the Pope in 1920.

At the end of the First World War, Prof. Turner had agreed to continue at Oxford the seismological work of John Milne. Miss Bellamy assisted Turner, and in this connexion spent some months in 1919 at Shide in the Isle of Wight in charge of Milne's instruments. This responsibility she continued when the improved Milne–Shaw seismographs were transferred first to the Boys's basement in the old Clarendon Laboratory and ultimately in 1928 to the University Observatory itself. Her great contribution to seismology lay, however, in the preparation of the *International Seismological Summary* (prior to 1923 the

Bulletin of the British Association Committee on Seismology). Her part was to collate the readings, in some cases measuring the original records, of earthquakes as recorded initially by 200, afterwards nearly 600, seismological stations throughout the world, and to maintain year after year a correspondence with these stations which did much to improve the accuracy of time-keeping. Originally, Turner computed the epicentres from these collated readings, but from 1923 a greater and greater part of this work was taken over by J. S. Hughes, now the director of the *International Seismological Summary* at Kew. From these epicentres and the computed residuals for each station Miss Bellamy then prepared the copy for the press and read the proofs. This work she continued until the transfer of the *Summary* to Kew in 1946, adding to it during Hughes's war service the computation of the epicentres for six quarterly issues of the *Summary*. Time also was found to prepare a catalogue of epicentres from the *International Seismological Summary* for the years 1925–30, and in 1936 a complete *Index Catalogue of Epicentres* for the years 1913–30 (Isle of Wight County Press) together with a frequently reproduced equal-area map showing the location of these epicentres on the Earth's surface. A brief account of this work with some of the original maps appeared in *Nature* (**143**, 504; 1939).

Dogged throughout her life by ill-health and working in discomfort for many years in an old wooden hut in the Observatory grounds, nothing was ever allowed to stand in the way of the quality and quantity of her work. It was only fitting that she should have been awarded an honorary M.A. by the University of Oxford, whose faithful servant she had been for so many years. Retiring in 1947, she spent her last years in Upwey, near Weymouth.

H. H. Plaskett

NEWS and VIEWS

Element 103, Lawrencium

The creation of lawrencium, the eleventh new man-made element beyond uranium (element 92), was announced on April 13 by the University of California and the U.S. Atomic Energy Commission. An isotope of this element was formed on February 14 by bombarding 3 μgm. of californium (element 98) with boron-10 or boron-11 nuclei in a heavy-ion linear accelerator at the Lawrence Radiation Laboratory of the University of California; the four nuclear scientists who carried out this experiment, Drs. A. Ghiorso, T. Sikkeland, A. Larsh and R. Latimer, propose to name the new element lawrencium in honour of the late Ernest Orlando Lawrence, inventor of the cyclotron and founder of the laboratory which bears his name. Californium, used as the target material, is made by the prolonged irradiation of trans-uranium elements in a nuclear reactor by the successive addition of neutrons. Since each new heavy element is more unstable than the one before, this procedure is inapplicable to the heaviest elements and heavy-ion bombardment is the only route whereby they may be created. In addition, the identification of the heaviest elements prepared in this way becomes progressively more difficult with increasing atomic number owing to their instability and to the very few atoms of the product which are formed. Although it may be possible to create one or two more new elements by this technique, it is improbable that elements beyond number 105 will be synthesized and satisfactorily identified.

Ministry of Aviation : Mr. J. R. Mills

Mr. J. R. Mills has been appointed head of the Radio Department, Royal Aircraft Establishment, Farnborough. Educated at the Grammar School, Kingston-on-Thames and King's College, London, he completed in 1939 the special honours course in physics. Shortly after war broke out Mr. Mills joined the Air Ministry Research Establishment, Dundee (formerly Bawdsey Research Station). It was here that he began his connexion with radar. Between 1940 and 1944 he divided his time between the Ministry of Aviation Radio Department, the Royal Aircraft Establishment and the Telecommunications Research Establishment, working throughout most of this period on the problems of secondary radar systems, mainly in the metric wave-bands. In 1946 Mr. Mills was a member of the team at the Telecommunications Research Establishment which had been set up to develop electronic systems for use in civil aviation, his particular interest lying in the development of distance measuring equipment. During this period his group was one of the first in the United Kingdom to investigate the use of overtone crystals as frequency substandards. In 1950 he returned to the military field and concentrated on techniques for measuring range to a very high order of accuracy. From 1952 he led a team set up in the Telecommunications Research Establishment to carry out research into new forms of airborne surveillance radar and, in particular, to exploit the new wave-band (*Q*) centred on a wave-length of 0·86 cm. During 1954–60 Mr. Mills was the superintendent in the Airborne Radar Department, Royal Radar Establishment (formerly Telecommunications Research Establishment and the Radar Research Development Establishment), in charge of research and development concerned with the offensive airborne operational needs of the Royal Air Force and Royal Navy. For a brief period commencing in October 1960 he was the assistant director at Ministry of Aviation Headquarters concerned specifically with the electronic problems of civil aviation.

Mr. J. H. Briggs

Mr. J. H. Briggs has been appointed director of electronics, research and development (civil aviation) in the Ministry of Aviation. Mr. Briggs was educated at King Edward's School, Birmingham, and obtained a major open scholarship in natural sciences at St. John's College, Cambridge, where in 1935 he graduated with honours in the Mathematical Tripos Part I and Natural Sciences Tripos Part II (physics). After a year and a half in the carrier communications development laboratory of the General Electric Co. he joined the Government service at the Royal Aircraft Establishment, where for three years in the Radio Department he was engaged on direction-finding research and development. On transfer to

the Air Ministry Research Establishment at Swanage in 1940 initial work on radar aerial systems led to anti-surface vessel development and then to a period of liaison work with Coastal Command to investigate the utilization of anti-surface vessel Mk. 2 and prepare for the introduction of centimetre anti-surface vessel for the Battle of the Atlantic. On return to the Telecommunications Research Establishment at Malvern a period in charge of test-gear development was followed at the end of the War by the organization and running of a research programme on microwave measurements in conjunction with the Radio Research Station of the Department of Scientific and Industrial Research. During this period he was for a time chairman of the Inter-services Radio Measurement Committee (later the Radio Electronic Measurements Committee).

In 1950 Mr. Briggs undertook a programme of work involving simulation and computation to establish a mathematical model of a homing test vehicle for comparison with the results of flight trials. In 1955 he became a superintendent in the Ground Radar Department, Radar Research Establishment, in charge of the development of data handling systems, and as such was intimately concerned with the overall design of air defence systems. These interests resulted in participation in extensive negotiations within the Nato framework in connexion with the co-ordination of European defence requirements—particularly in the field of military data-processing and exchange. The recently renewed interest in co-ordination of defence and air traffic control requirements brought him into close touch with civil aviation problems so that he is particularly well qualified for his new appointment.

United Kingdom Atomic Energy Authority Appointments

The Atomic Energy Authority and the National Institute for Research in Nuclear Science have agreed that the development of particle accelerators hitherto carried out by the Accelerator Division, Atomic Energy Research Establishment, Harwell, should be the responsibility of the Rutherford Laboratory of the National Institute for Research in Nuclear Science. Mr. L. B. Mullett, the head of the Accelerator Division, has joined the Rutherford Laboratory as assistant director for accelerator and applied physics. Other appropriate staff transfers have already been made.

Consequent on the appointment of Dr. R. Spence as deputy director of the Atomic Energy Research Establishment, Harwell, Dr. W. Wild has been appointed head of the Chemistry Division. He has responsibility for the scientific work of three branches: Chemical Processing and Reactor Chemistry; Radiation Chemistry and Solid State Chemistry; Radiochemistry. Mr. A. A. Smales, head of the Analytical Chemistry Branch, has been given the status of a division head and will be directly responsible to the director of the Establishment for the scientific work under his control. His branch will continue to use the general administrative services of the Chemistry Division.

Day-release Students in England and Wales

In a written answer in the House of Commons on April 14, the Minister of Education, Sir David Eccles, gave the number of day-release students under 18 years of age enrolled in major establishments of further education in England and Wales in 1959–60 as 191,526 boys and 50,976 girls. Of these, 91,009 boys and 23,419 girls were in the English counties (including London), and 91,070 boys and 26,247 girls in the English boroughs; only 6,501 boys and 857 girls were in the Welsh counties, and 2,946 boys and 453 girls in the Welsh boroughs.

Educational Statistics for England and Wales

As a complement to the national statistics which appeared in his annual report, "Education in 1959", the Minister of Education has now issued a wide range of statistical material concerning local education authorities in England and Wales (Selected Statistics relating to Local Education Authorities in England and Wales, Educational Year 1958–1959. Pp. ii+25. (London: H.M. Stationery Office, 1960.) 3*s.* net). The booklet contains estimates of the total population of the two countries and statistics of the total number of scholars in primary and secondary schools, and in training colleges in counties and county boroughs in England and Wales. There is also interesting information about the number of medical officers, dental officers and nurses serving each local authority; the number of pupils receiving milk and school meals; the number of awards made by local authorities to students wishing to study at a university or elsewhere—the latter show that sufficient discrepancies occur to make implementation of the full recommendations of the Anderson Committee a matter of urgent necessity.

U.S. Project Mohole

The National Academy of Sciences and the National Science Foundation announced recently that the experimental drilling ship, *Cuss I*, operating in 12,000 ft. of water off the west coast of Mexico in the Project Mohole, obtained, for the first time, a sample of the so-called second layer under the softer sediments of the ocean floor. This layer, the presence of which has been previously known only by reflexions of seismic soundings, has been revealed as basalt. This hole, which was begun at Guadalupe Island on March 31, reached a depth of 490 ft. after 11 hr. of drilling. Coring then began, and cores of soft, grey-green clay of Miocene age were obtained to a depth of 560 ft. At that depth the drilling-rate abruptly decreased and when the core barrel was retrieved, it was found to contain a hard, fine-grained basalt; the drilling had achieved threshold to the sima.

Animals for Cancer Research

The provision of animals for cancer research was discussed at a symposium sponsored by the Laboratory Animals Centre of the Medical Research Council Laboratories on May 23, 1960. Discussion was mainly concerned with the desirability of providing suitable animals from a central organization or whether users should provide their own locally. The dilemma was posed by Prof. J. S. Mitchell, of the University of Cambridge, who acted as chairman of the symposium, and indicated that the provision of animals for research needs expert knowledge, including that of mammalian geneticists and veterinary experts. The problem is not only one of size but also involves many technical problems, including, for example, continued testing to make certain the strains are authentic, and maintenance of the production of disease-free animals. The great contribution to cancer research has been the develop-

ment of inbred strains of animals, especially mice, and the use of *F*1 hybrids between two inbred strains. At the present time, about eighty inbred strains of mice are known. Much less seems to be known about the genetics of rats. There are a few, perhaps not more than five, pure strains of rats. It is questionable whether the maintenance of all these strains, that is, about eighty inbred strains of mice and perhaps five inbred strains of rats, is necessary for cancer research. Prof. Mitchell believes that there is need to establish a large organization with expert staff and proper financial support to provide animals and tumours needed for cancer research. A full report of the symposium has now been published by the Centre (Collected Papers, Vol. 9, 1960. Pp. 116. Carshalton, Surrey: Laboratory Animals Centre, Medical Research Council Laboratories, 12*s*. 6*d*.).

Paranormal Phenomena

Although almost all physiologists regard the brain as in some sense the 'organ of mind', it has to be admitted that our knowledge of its action is still distressingly incomplete. In his fourteenth Frederic W. H. Myers Memorial Lecture, Dr. W. Grey Walter provides a most useful survey of recent work on the neurophysiological aspects of hallucinations and illusory experience (*The Neurophysiological Aspects of Hallucinations and Illusory Experience*. Pp. 24. (London: Society for Psychical Research, 1, Adam and Eve Mews, W.8, 1960.) 2*s*. net). As he points out, it is now possible to evoke by experimental techniques a variety of bizarre subjective states long thought to be peculiar to epilepsy or kindred nervous disorder. These techniques include rhythmic photic stimulation, sensory deprivation and the use of psychotomimetic drugs; the results obtained go far to justify Dr. Grey Walter's hope that many phenomena formerly consigned to the occult may come to achieve reputable neurophysiological explanation. At the same time, he finds little to say about those aspects of hallucinations which particularly interested Myers, such as their occasional (though apparently well-authenticated) telepathic character. It would seem, then, that neurophysiology has still far to go before it can provide an acceptable explanation of paranormal phenomena.

The Raffles Museum, Singapore

The Bulletin of the Raffles Museum, Singapore (No. 26; February 1961), maintains the high standard of research results that is now associated with this well-known publication. All the papers deal either with zoological or palæontological subjects based on Malaya and are well and clearly illustrated. An interesting experiment relates to an attempt to hatch the eggs of the leathery turtle, and a brief account of the geology of the limestone hills of Malaya is an important contribution to the stratigraphy of the region.

Museums Association: Monthly Bulletin

After publishing the *Museums Journal* each month for 60 years without a break it has now been decided to issue a monthly *Bulletin* and a quarterly *Journal*. The first issue of the former (No. 1, April 1961) has just appeared. It is a 4-page production giving essential and current museum news and notices, obituary notices, recent appointments, letters to the editor, a list of temporary exhibitions in certain museums and details of posts now vacant in museums and art galleries.

'Araldite' in Museum Work

Technical Notes, No. 218, issued by C.I.B.A. (A.R.L.), Ltd., gives some interesting examples of the use of 'Araldite' in the numerous problems confronting museum staffs ('Araldite' in Museum Work. Pp. 10. Duxford: C.I.B.A. (A.R.L.), Ltd.; February 1961). The resin can be used either to assemble broken and fragile articles or to reinforce and consolidate museum objects and thus preserve them for posterity. The examples quoted include the Kentmere boat unearthed in Westmorland during 1955 strengthened by the use of a formulation consisting of 'Araldite' *CY* 219 (50 parts), hardener *HY* 219 (25 parts), accelerator *DY* 219 (1 part) and dibutyl phthalate (10 parts). Other objects dealt with in a somewhat similar manner were a Nigerian ceremonial mask, the St. Ninian's hanging bowl dating from about A.D. 800, and a Belgic wrought-iron frame. Other museum objects quoted are from the Royal Scottish Museum, Edinburgh, where repair work with 'Araldite' has been carried out with success including colour matching if the glue line is rather wide.

Poultry Keeping

Keepers of fowls, ducks and geese will welcome the publication by the Ministry of Agriculture, Food and Fisheries of its two Bulletins on these birds. One of these, entitled *Poultry Breeding* (Bulletin No. 146. Third Edition. Pp. vi+146. By G. E. Mann. London: H.M.S.O., 1960. 7*s*. net), contains 146 pages of valuable information written by G. E. Mann, poultry advisory officer of the National Agricultural Advisory Service, on the genetics of poultry, the inheritance of breed and economic characteristics and on mating systems and systems of breeding, with a glossary explaining technical terms. One of its aims is to give the smaller breeder practical information about the methods used by the larger breeders. The other Bulletin, entitled *Ducks and Geese* (Bulletin No. 70. Pp. v+93+8 plates. Fourth Edition. London: H.M.S.O., 1960. 6*s*. net), will interest those who find that these birds are not only interesting in themselves, but also profitable either as a large-scale enterprise or as a side-line. Their rate of egg production and of food conversion is high, and this Bulletin takes the reader step by step through the intricacies of choosing a good breed, methods of breeding, management, rearing and fattening, and of the marketing of eggs and birds. There is also some information about by-products, and the diseases of ducks and geese and their prevention and control. Written by experienced contributors, this Bulletin provides sound, practical advice. It has five appendixes on nutrition, the preparation of the birds for the oven, feeding trials, losses of weight due to plucking and trussing ducklings and a summary of the main breeds and their characteristics. Its eight pages of excellent photographs include portraits of ten breeds and pictures of how to handle birds when they are being sexed. Its twelve line-illustrations are all also of practical value.

Test on Recording Spectrophotometers

The Photoelectric Spectrometry Group is organizing a collaborative test on commercially available recording ultra-violet spectrophotometers which will be based, so far as possible, on the successful test on manually operated instruments that was reported in the *Photoelectric Spectrometry Group Bulletin*

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Volume II edited by R. GOODMAN

This is the second volume of the authoritative annual series published for the Automatic Programming Information Centre. Included are two main groups of papers: one concerned with problems of languages for scientific computation, and the other with problems of a common business data-processing language. In this second group of papers is reflected the trend of present controversy about the value of COBOL as such a language.

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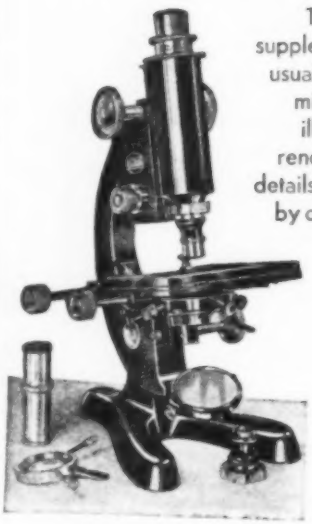

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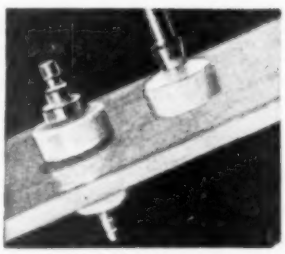

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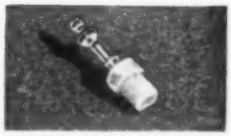

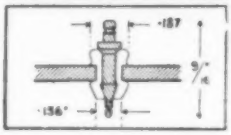

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No. 4 (1954). A pilot run to establish the conditions of the test has been successfully conducted on approximately 10 instruments of 5 different makes. It is hoped that as many separate examples of all commercially available instruments can be included in the full-scale test, which it is expected will be initiated in October of this year. Sample solutions will be supplied to those who agree to enter the test and they will be asked to run spectra (*a*) under predetermined instrumental conditions, (*b*) under their own preferred conditions. The analysis of the results of the test will be published in the *Bulletin*. Anyone who would like to enter a recording ultra-violet instrument should write to the honorary secretary, K. A. Macdonald, Unicam Instruments, Ltd., Arbury Works, Cambridge.

The Devon Naturalists Trust

A BODY, to be known as the Devon Naturalists Trust, has been formed with the support of many national and local bodies including the Nature Conservancy, the Council for Nature and the Devonshire Association. Lord Roborough is to be president of the Trust, and Mr. H. G. Hurrell chairman of its executive committee. The aims of the Trust are to protect places of interest to naturalists, to preserve the county's wild-life against encroachment, and to encourage the study of natural history. These aims should appeal to many who are concerned at the tide of change that has already much reduced the natural amenities of other counties, and is beginning to do so in Devon, too. It will be one of the main concerns of the Trust to see that developments of this sort are kept under constant review. There will be a meeting in Exeter to invite support and to publicize the Trust on May 16. Further information can be obtained from the honorary secretary, C. P. E. Grant, Chain House, Modbury, Ivybridge, Devon.

Grants for Field Work in Natural History

AT the suggestion of the Council for Nature, the Carnegie United Kingdom Trust has set aside a fund from which it will make grants to approved societies for assistance with field work. These grants will be made on recommendations submitted by the Council for Nature, and will be contributions towards expenditure incurred in carrying out specific projects that give amateurs experience of field work in natural history under skilled direction. Approved expenditure is likely to include fees paid to experts for instruction and leadership, the incidental expenses of such people and the cost of essential equipment subject to certain conditions. Grants will not be available for the expenses incurred by members of the societies taking part in any scheme or for the general support of a society. Full particulars of the conditions for the award of grants can be obtained from the Council for Nature, 41 Queen's Gate, London, S.W.7.

Library of Recorded Animal Sounds

A LIBRARY of recorded animal sounds is being set up by the Committee for Biological Acoustics in collaboration with the British Institute of Recorded Sound, 38 Russell Square, London, W.C.1, in the archives of which the records will be stored. The records will be made on magnetic tape and recorded at a standard speed of 7½ in. per sec.; each record will contain a commentary giving physical and biological data in relation to the recording. The recordings will be available free on loan to bona fide research workers anywhere in the world and the only expenses will be postage of the tapes. The library is being supported by a grant for equipment from the Royal Society. As soon as a reasonable number of recordings have been amassed a catalogue will be prepared and sent free of charge to all interested workers, departments and institutions. It is hoped that all workers in the field will give their support to the project, and those willing to allow their recordings to be copied for the library are asked to write to Dr. P. T. Haskell, Committee for Biological Acoustics, c/o Anti-Locust Research Centre, 1, Princes Gate, Kensington, London, S.W.7.

Japan Association for Study of Congenital Anomalies

THE Japan Association for Study of Congenital Anomalies held its initial meeting at the Kyoto University, Faculty of Medicine, on February 25, 1961. For the time being, the Association has been established on an informal basis, by an organizing group consisting of the following members: Prof. Chisato Araki (Kyoto University); Prof. Tameyoshi Baba (Osaka Municipal University); Prof. Ichiro Hayashi (Nagasaki University); Prof. Yoshiki Mikami (Mie Prefectural University); Shigeru Mitani (Tokyo Women's Medical College); Prof. Ujihiro Murakami (Nagoya University); Prof. Hideo Nishimura (Kyoto University). Prof. Nishimura and a member of the organizing group will be in charge of international affairs.

Association of Consulting Scientists

AT the annual general meeting of the Association of Consulting Scientists, held in London recently, the following honorary officers and members of council were elected: *chairman*, Dr. M. Barent (Barent and Johnson); *vice-chairman*, Mr. F. G. Sarel Whitfield (Avebury Research Laboratories, Ltd.); *honorary treasurer*, Dr. G. W. Ferguson (Parry and Ferguson); *honorary secretary*, Mr. W. H. Stevens (W. H. Stevens); *members of council*, Dr. H. H. Chambers (Sondes Place Research Laboratories, Ltd.), Dr. J. G. Davis (Dr. J. G. Davis and Partners), Dr. Julius Grant (Hehner and Cox, Ltd.), Dr. R. F. Milton (R. F. Milton), Mr. O. W. Roskill (O. W. Roskill).

1961 Waverley Gold Medal Essay Competition

THE Waverley Gold Medal essay competition is sponsored by *Research* to encourage scientists to write clearly and comprehensibly about their work. The Medal, together with £100, will be awarded for the best essay of about 3,000 words describing a new project or practical development in pure or applied science, giving an outline of the scientific background, the experimental basis and the potential or actual application of the idea to industry or its importance to society. A second prize of £50 will be awarded and also a special prize of £50 for the best entry from a competitor under the age of thirty on July 31. Entry forms and further information can be obtained from the Editor of *Research*, 88 Kingsway, London, W.C.2. The last date of entry is July 31.

Film-Strips on Physical Science

A CLASSIFIED list of their film-strips and wall-charts in physics, chemistry and general science has been issued by Educational Productions, Ltd., of East Ardsley, Wakefield, Yorks. The strips deal with such topics as the structure of matter, electricity and light, while there is also a whole series of wall-

charts linked to the products of prominent industrial organizations and produced in collaboration with them. Wall charts are also available to describe lessons in astronomy and space exploration.

Guide to Careers

As a link with the Commonwealth Technical Training Week which is to be held during May 29–June 4, the 1961 edition of the *Guide to Careers* published by the National Union of Teachers is mainly concerned with the training of young people in industry and commerce (Pp. viii+80. London: National Union of Teachers, 1961). In a foreword to the Guide, H.R.H. the Duke of Edinburgh directs attention to the need for careful choosing of careers. Many experts describe the different careers available to young people, and these are supported by even more advertisements in which the advantages of a particular company or organization are displayed. School-leavers themselves are likely to find the mass of generalizations somewhat overwhelming, and will seek refuge in the related experiences of some young people who have already tried out certain jobs for themselves. Even these tend to be over-glamorized and should be balanced by descriptions from young people with experience of jobs somewhat more mundane than that of staff manageress or management trainee.

Postgraduate Courses in London

Particulars of full-time postgraduate courses of one or two years duration which lead to a degree or diploma are contained in a booklet *Postgraduate Courses*, 1961–62, issued by the Imperial College of Science and Technology (Pp. xii+114. London: Imperial College of Science and Technology, 1961). These courses, which have been accepted by the Department of Scientific and Industrial Research as suitable for the tenure of advanced course studentships, are indicated, and besides outlining the content of the individual courses, their length and the respective lecturers, the booklet includes the regulations for the diploma of the Imperial College of Science and Technology.

Gordon Research Conferences 1961

The Gordon Research Conferences have justly achieved international fame as effective instruments for the exchange of ideas and information between research scientists drawn from industrial, Government and academic laboratories, and the organizers have been paid the great compliment of having their methods copied in other countries. Papers are presented at morning and evening sessions over a period of four and a half days and the formal programme is often very slight, for example, in the 1961 Petroleum Conference only six papers are scheduled for formal presentation. There is ample time for discussion, the environmental and residence conditions are all favourable and the selected membership ensures that the discussion is free and of a high level. As in previous years a conference will be held each week during June 12–September 1 at each of three residential schools in New Hampshire, and the subjects cover a wide range in the physical and biological sciences. Residence and registration charges for a week amount to 100 dollars. Further information can be obtained from Dr. W. George Parks, Department of Chemistry, University of Rhode Island, Kingston, R.I. Applications for attendance should be submitted before June 12.

University News:

Bristol

The following appointments to senior lectureships have recently been announced: Mr. R. Bassindale (zoology); Dr. A. Couper (inorganic and physical chemistry); Dr. F. G. Hannell (geography); Dr. J. R. Holmes (veterinary medicine); Dr. W. K. Metcalf (anatomy); Mr. W. H. Dearden (metallurgy); Dr. M. S. G. Cullimore (civil engineering).

Cambridge

The Arnold Gerstenberg studentship for 1962 is open to students in the University of Cambridge who, going into residence not earlier than 1956, have obtained honours in the Natural Sciences Tripos and who wish to pursue a course of philosophical study. The studentship will be awarded for an essay, which must be submitted before May 1, 1962. Further information can be obtained from Mr. Gerd Buchdahl, Whipple Science Museum, Free School Lane, Cambridge.

London

The following announcement has been issued by the Imperial College of Science and Technology: Prof. D. M. Newitt, pro-rector and head of the Department of Chemical Engineering and Chemical Technology, who retires on September 30, has been appointed senior Research Fellow of the College. Prof. P. M. S. Blackett has been appointed pro-rector as from October 1, and Prof. A. R. Ubbelohde as head of the Department of Chemical Engineering and Chemical Technology. The following have been elected Fellows of the College: Prof. O. M. B. Bulman, Woodwardian professor of geology, University of Cambridge; Prof. A. C. Chibnall, professor emeritus, former professor of biochemistry; Mr. T. G. N. Haldane, member of the Governing Body of the College; Dr. D. T. A. Townend, director-general of the British Coal Utilization Research Association; Dr. J. H. Watson, chief assayer, Royal Mint.

Dr. A. H. Chilver, a director of studies in engineering, University of Cambridge, has been appointed to the Chadwick chair of civil engineering tenable at University College. Dr. F. G. Bailey, lecturer in Asian anthropology at the School of Oriental and African Studies, has been appointed to the University readership in Asian anthropology tenable at that School. Dr. E. G. Gray, lecturer at University College, has been appointed to the University readership in cytology tenable at that College.

Titles have been conferred as follows: Sir William Collins professorships, on Mr. G. W. Causey (anatomy) and Dr. G. J. Cunningham (pathology) in respect of the posts held by them at the Institute of Basic Medical Sciences; reader in veterinary physiology at the Royal Veterinary College, on Dr. F. R. Bell; reader in anatomy at St. Mary's Hospital Medical School, on Dr. A. S. Breathnach; reader in physics at University College, on Dr. F. F. Heymann; reader in chemistry at University College, on Dr. J. Lewis; reader in chemical engineering at University College, on Dr. J. W. Mullin.

Sheffield

The title of Dr. G. Weber's readership has been announced as reader in biophysics. J. E. Enderby has been appointed as a lecturer in physics; and Dr. J. V. S. Mani has been appointed an Imperial Chemical Industries research fellow in the Department of Fuel Technology and Chemical Engineering.

Southampton

The origins of the University of Southampton lie within the Hartley Institute, established from a bequest by H. R. Hartley in 1862. Towards the University's centenary appeal, Hawker-Siddeley Aviation, Ltd., is contributing a sum of £28,700, over a period of seven years, for a readership and a lectureship in the Department of Aeronautics and Astronautics; Alcan Industries, Ltd., is contributing a sum of £10,000.

The title of senior lecturer has been conferred on Mr. K. N. C. Bray (aeronautics and astronautics), Dr. W. A. Gambling (electronics), Dr. N. S. Grassam (mechanical engineering) and Dr. A. C. Riddiford (chemistry). The following new appointments have been made: Mr. V. J. D. Baston, Dr. H. Holstein and Mr. C. R. F. Maunder (lecturer in mathematics); Mr. W. S. Hall and Mr. T. Sprinks (Research Fellows in mathematics); and Mr. G. C. Spencer (lecturer in mechanical engineering).

Announcements

Sir Harold Roxbee Cox, formerly chief scientist of the Ministry of Fuel and Power and at present chairman of the Metal Box Co., Ltd., has been appointed chairman of the Council for Scientific and Industrial Research for five years from October 1, 1961, in succession to Sir Harry Jephcott, who completes his term of office in September.

Miss M. J. Bishop, headmistress of the Godolphin and Latymer School, Hammersmith, has been appointed a member of the University Grants Committee in succession to Dame Kitty Anderson, who resigned from the Committee on her appointment as a member of the Committee on Higher Education. Miss Bishop's appointment runs to December 31, 1963.

The United Nations Food and Agriculture Organization is organizing a technical meeting on "Plant Exploration and Introduction", to be held in Rome during July 10–20. Further information can be obtained from the Food and Agriculture Organization, Viale delle Terme di Caracalla, Rome.

A technical meeting of the United Nations Food and Agriculture Organization to discuss "Plant Exploration and Introduction" is to be held during July 10–20, at the headquarters of the Organization in Rome, from which further information can be obtained.

The summer conference of the Society for Applied Bacteriology will be held at Wye College, Kent, during July 11–13. Included in the programme is a symposium on "Bacteria of the Intestine". The conference is open to all, and further information can be obtained from Dr. Ella M. Barnes, Low Temperature Research Station, Downing Street, Cambridge.

The second congress of the International Federation of Societies of Cosmetic Chemists, organized by the Society of Cosmetic Chemists of Great Britain, will take place in London during July 2–5. Further information can be obtained from A. Herzka, c/o Pressurized Packaging Consultants, Ltd., Ashbourne House, Alberon Gardens, London, N.W.11.

The sixty-sixth annual congress of the South-Eastern Union of Scientific Societies will be held at Haslemere, Surrey, during May 26–28. The theme of the congress will be "The Changing Country-side" and the programme will include a number of lectures, a brains trust and various excursions. Further information can be obtained from the general secretary and treasurer, Frank Edwards, 53 The Drive, Shoreham-by-Sea, Sussex.

The eighth International Cancer Congress will be held in Moscow during July 22–28, 1962, under the auspices of the International Union against Cancer. The Congress will meet at the Moscow State University and will consider both experimental and clinical aspects of the problem. Further information can be obtained from the general secretary of the Soviet National Organizing Committee, Prof. L. Shabad, or the assistant general secretary, Dr. N. Perevodchickova, Academy of Medical Sciences of the U.S.S.R., 14 Solyanka, Moscow.

An international exhibition, devoted to measurement control, regulation and automation, is being held in Paris during May 9–17. The exhibition is being organized by the MESUCORA Association in conjunction with the Fédération des Industries Mécaniques et Transformatrices des Métaux, the Syndicat Général de la Construction Electrique, and the Fédération des Industries Electroniques. This event will also include the annual exhibition of the Société Française de Physique. Further information can be obtained from Congress International, MESUCORA, 40 Rue du Colisée, Paris, France.

Hatfield Technical College is organizing a series of lectures on the general theme "Technology, Science and Art—Common Ground". The details are as follows: "Science in History" by Prof. J. D. Bernal (May 5); "Poetry and Science" by T. R. Henn (May 12); "Science and Ethics" by Dame Kathleen Lonsdale (May 26); "Science and the Classics" by Prof. B. Farrington (June 2); "Art and Engineering" by Prof. M. Black (June 23). All lectures will be held in the Old Library of the College on the dates indicated. Further information can be obtained from Mr. I. O. McLuckie, chairman, Teaching Staff Association, Hatfield College of Technology, Hatfield, Herts.

The 1961 Conference on Medical Electronics, which is to be held at the Waldorf Astoria Hotel, Park Avenue and 49th Street, New York City, N.Y., during July 16–21, will be a combined meeting of the fourth International Conference on Medical Electronics and the fourteenth Annual Conference on Electrical Techniques in Medicine and Biology. It is to be sponsored by the Joint Executive Committee on Medicine and Biology under the auspices of the International Federation for Medical Electronics, and is organized by the Institute of Radio Engineers. Further information can be obtained from the Secretary-General, Fourth International Conference on Medical Electronics, Institute of Radio Engineers, 1 East 79th Street, New York 21, N.Y.

A course in tropical hygiene for laymen will be held by the Ross Institute during July 3–7. The course is designed specially for planters, mining engineers and other non-medical people who may be responsible for the health of industrial labour forces in the tropics. Admission is not restricted to such people, however, but is open to any non-medical men and women proceeding to the tropics. Further information can be obtained from L. G. Ponsford, organizing secretary, Ross Institute of Tropical Hygiene, London School of Hygiene and Tropical Medicine, Keppel Street (Gower Street), London, W.C.1.

MALNUTRITION

ON March 18, the Nutrition Society held, at the London School of Hygiene and Tropical Medicine, a symposium on "The Place of Food Science and Technology in the Campaign against Malnutrition". The symposium was primarily concerned with malnutrition in the under-developed countries, and in particular with malnutrition in children in the 'toddler' stage.

There is much evidence that malnutrition associated with lack of protein and calories is common in countries in which supplies of foods of animal origin, especially animal milk, are low; it is, in fact, the most common of all food deficiency states in the world as a whole. Its manifestations range from retardation in growth to serious disease and death. The West African word 'kwashiorkor' is now widely used to describe a form of the disease, with characteristic signs, occurring in children whose diet is grossly deficient in protein and less deficient in calories. The wider term 'protein calorie malnutrition', covering the effects of both lack of calories and lack of protein, usually found together in the victims, is preferred by many workers, but it should be added that at present there is some confusion with respect to nomenclature.

As the result of intensive research during the past ten years in many parts of the world, the factors underlying protein calorie malnutrition—dietary, agronomic, economic and social—are now well understood, but relatively little progress has as yet been made in prevention. Through food science—meaning in this context the study of foods and food values in relation to requirements—appropriate measures for correcting deficiencies can be demonstrated, and food technology, wisely applied, can increase supplies of nutritious foods pending, and in association with, the expansion of food production.

The symposium began with five papers, under the heading of "Problems and Some Solutions", given by workers from India (Dr. K. K. Halder), Turkey (Dr. O. Köksal), Iraq (W. Frankul), Pakistan (S. M. Ali) and Ghana (R. Orra ca-Tetteh) respectively, who are engaged in research at the Human Nutrition Research Unit at Mill Hill, under the direction of Prof. B. S. Platt. Each speaker outlined the background of the problem in his country and described some locally feasible method or methods, based on recent research, of making diets more satisfactory. These papers brought out on one hand the basic similarity of the situation in various parts of the world, and on the other, the differences from country to country which call for a local approach in applying food science and technology effectively. In introducing these contributions, Prof. Platt commented on the value of providing postgraduate experience in nutrition research and its application to workers from countries in which there are serious problems of nutrition and a shortage of trained personnel to deal with them.

A paper on "Some African Problems" by Dr. F. Aylward (Department of Chemistry and Food Technology, Borough Polytechnic, London) reflected the author's experience as adviser to the Ministry of Agriculture in Ghana in the capacity of a technical assistance expert for the Food and Agriculture Organization. He analysed the contributions which food technology can make in increasing supplies of nutritious foods available for consumption, suggesting various categories into which these contributions can be grouped. His paper was concerned with the application of food technology in ways which do not demand big capital outlay, rather than with the development of large-scale food industry. He considered that under African conditions there is an important place for small food-processing plants in rural areas, with low maintenance costs and minimum requirements for technical supervision. Dr. J. W. Corran (J. and J. Colman, Ltd., Carrow Works, Norwich), who dealt with "Factors Affecting Development of Food Science and Technology and Food Resources in Pakistan", also drew on experience gained during a Food and Agriculture Organization assignment as a technical assistance expert. He directed attention to the lack of accurate data about food consumption and state of nutrition and of reliable agricultural statistics, which handicapped attempts to formulate and execute programmes to develop food production and food technology. For example, there were widely conflicting estimates of supplies of fish, an important food in East Pakistan. While Pakistan greatly needed trained food scientists and technologists, the number of active workers in these fields could at present be counted on the fingers of one hand. Facilities for training such workers in Pakistan did not exist, and even those available in the United Kingdom were far from satisfactory. Pakistan urgently needed the help of food technologists from abroad to foster the growth of food industry.

Dr. E. Wokes (Vegetarian Nutritional Research Centre, Research Laboratory, Stanborough School, Watford, Herts) discussed "India's Food Problems" on the premise that substantial increase in supplies of animal protein could not be expected in the foreseeable future. Attention must therefore be focused on plant proteins, which are cheaper than animal proteins, and may be obtained from pulses, groundnut preparations, leaf protein concentrates, and other sources. The lack of vitamin B_{12} in plant proteins might be corrected by fortification with the synthetic vitamin itself. He referred to deficiencies of lysine and methionine in average Indian diets and to possibilities of making these good by suitable combinations of vegetable foods. In conclusion, he stressed the need for more clinical and nutritional research, and for developments in food technology, food control, agriculture, transport and education.

An account was given by Dr. W. F. J. Cuthbertson (Glaxo Laboratories, Ltd., Greenford, Middlesex) of "The Commercial Development of 'Amamu', a protein-rich Supplement in Nigeria". This preparation, based on groundnut flour to which casein, yeast, minerals and vitamins are added, is manufactured in a factory near Lagos. Tests made in Nigeria, where protein malnutrition is common, showed that 'Amamu' was as effective in treating malnourished children as skim milk powder. Cuthbertson emphas-

ized that the manufacture and distribution of a new food to wholesalers and retailers were not enough to ensure its use; an advertising and educational programme was essential so that the public can become aware of its availability and how to use it. He outlined the methods followed in promoting the sale of 'Amamu', and the difficulties encountered.

Throughout the symposium there were many references to the need for popular education in nutrition, which must accompany all other measures to eliminate malnutrition. The last paper, by Dr. A. T. M. Wilson (Unilever House, Blackfriars, London), on "Nutritional Change; Some Comments from Social Research", dealt mainly with this subject. He quoted effectively a passage in a World Health Organization report about the "baffling maze of tradition, taboo and magic, and the whole system of belief of the people about health and the causes of disease" of which educators must be aware. "In the past", the World Health Organization report continued, "most workers have tried, by repeated blows of didactic teaching, to hammer their way through the maze and break down the resistance to unaccustomed foods and eating practices—with very little success . . . because beliefs about food are part of the whole fabric of the life of a people". It follows that the social and psychological aspects of the campaign against malnutrition are of essential importance, an example being the complex social factors which influence lactation and weaning. Wilson also commented that the campaign called for co-operation between different disciplines and services, always difficult to secure. The epigram "God has not seen fit to divide our problems into the same categories as university chairs" was highly applicable to the problem of nutrition.

The papers and discussions at the symposium gave at least some answers to the questions implied in its title. While the general attitude was optimistic, the speakers recognized that immediate and facile solutions cannot be expected. There was emphasis on the need for action based on research and on an understanding of the complex factors which cause malnutrition.

W. R. Aykroyd

GROWTH AND GENETICS OF HIGHER FUNGI

THE higher fungi commonly known as mushrooms, toadstools and bracket fungi and classified in the Basidiomycetes, have certain distinctive biological features which make them a favourable group in which to study their physiology of growth and their genetics. The large fruiting body with its size, shape and form, and in many species with its extraordinary rate of growth, offers opportunities for studying the factors affecting growth, translocation and morphogenesis. The mycelium with its regular growth-pattern, its production of asexual spores and its ability to grow on simple minimal medium has all the properties of mycelia in other groups of lower fungi. The regular formation of a stable dikaryon from the compatible mating of monokaryons provides a system for studying gene action which is intermediate between the regular haploid diploid cycle of yeast and the variable heterokaryon and homokaryon in *Neurospora* and *Aspergillus*. The complex mating system in the higher fungi, although it can be compared in its genetics with certain incompatibility systems in higher plants, has features that are not found in any other group of plants.

In a symposium organized by the British Mycological Society, under the chairmanship of its president, Miss G. M. Waterhouse, five aspects of the higher fungi were examined: (1) the effects of light and gravity on the growth and form of a fruiting body; (2) the factors, both internal and external to the hyphæ, which govern the regular pattern of growth and branching of the mycelium; (3) the extent of gene action and the transport of exogenous substances along the hyphæ; (4) the genetic and possible biochemical control of the complex mating system; (5) the mosaic structure of populations and sterility barriers in higher fungi.

Dr. B. E. Plunkett (Birkbeck College, London), using the fruiting-bodies of *Polyporus brumalis*, demonstrated components of the complex system of stimuli that operate to keep the cap horizontal and to ensure the production of spores on the lower side. These are factors of importance if the fungus is to distribute its spores efficiently. The stalk of the young fruiting body, before the cap has expanded, grows towards a laterally placed light, but as the cap expands it is no longer attracted to the light but grows upwards under the influence of gravity on the horizontal stem. Light of low intensity obtained by shading the young stem with an artificial cap resulted in upward growth due to gravity. This showed that the geotropic response was present in the early as well as in the later stages of development. The weaker geotropic response is at first overruled by the strong photo-response, but later, as the perceptive region is shaded by the expanding cap, the geotropic response expresses itself. Rotation-with-light experiments demonstrated that the spore-bearing region develops away from the light and the cap develops at right angles to the incident light. These interesting studies in growth and morphogenesis were paraphrased by the statement that according to Corner the cap was an umbrella to keep rain from the spores, but now it could also be a parasol.

Turning from the fruit body to the mycelium, Dr. G. M. Butler (Birmingham) discussed the problems of the hyphal branching system in *Coprinus disseminatus*. Three types of hyphæ could be distinguished, main, primary branch and secondary branch. In Petri dish cultures the main hyphæ had the highest extension-rate and the greatest diameter, the secondary branch had the lowest rate and diameter. The monopoidal branching system and the radial growth of a colony depend on these differential extension-rates of leading and branch hyphæ. A steady rate of growth of a whole branch system is maintained, from which it is concluded that the hyphal tip, the region where extension occurs, is not autonomous but is subject to competition and interaction occurring within the hyphal system. Experiments with two cultures separated by 'Cellophane' and growing out of step showed that under certain conditions there existed hyphal competition or

inhibition transmitted in the culture media, but this external effect, even at its greatest intensity, was too small to account for the difference between the main and branch hyphæ in extension-rate and diameter. Little is known about the main control of hyphal growth, which is internal, either in its extent along the hyphæ or in its mode of action, but it appears to operate on cell extension rather than on nuclear division.

Prof. D. Lewis (University College, London) discussed the problem of hyphal tip autonomy from a genetical approach and came to the same conclusion that the tip is not autonomous. A methionine-requiring mutant *me*-1 of *Coprinus lagopus* produced prototrophs not requiring methionine at a frequency of 2 in 10^5 asexual spores. These asexual spores are uninucleate and are cut off from the tips of hyphæ. The prototrophs are the result of recessive mutants of suppressor genes. Monokaryotic mycelia of the *me*-1 stock, when transplanted to minimal media, do not produce prototrophic sectors of growth despite the fact that hyphæ grow for 1 mm. into the minimal medium. The recessive mutant therefore is not expressed in the articulated hyphæ but is expressed in the isolated spore.

A dikaryon which is homogenic for *me*-1 and heterogenic for a suppressor gene will not grow on minimal medium, but each hypha resolves into a monokaryon with the nucleus carrying the suppressor gene. This difference between the monokaryon and dikaryon indicates that the sphere of gene action extends well beyond its own cell in a monokaryon, but in a dikaryon the same gene has a limited field of action and may be limited to its own cell. Experiments on the transport of exogenously supplied methionine in monocaryons and dicaryons did not reveal any difference between the two types of mycelia. Transport was limited to 1–3 mm. in both; this is a fact which may have a direct explanation for the lack of fruiting ability of many biochemical mutants when homogenic.

The unique mating system in the higher Basidiomycetes is controlled by two genetic loci *A* and *B*; one gene controls the migration of the donor nucleus in the receptor hyphæ and the other gene controls the regular synchronous division of the two nuclei and the formation of the clamp connexions which are peculiar to the Basidiomycetes. The *A* and *B* loci in *Schizophyllum commune* have been analysed into two genes in each.

Dr. P. R. Day (John Innes Institute) described a genetical analysis of the *A* complex in *Coprinus lagopus*. Using two auxotrophic mutants linked on both sides of the *A* locus, recombinants of the outside auxotrophic mutants were selected on minimal medium, and among these were a few *A* alleles which were different from the two parental alleles. The frequency of recombination to give these new alleles was 0·07 per cent. The recombining parts have been called sub-units; but whether these sub-units can be considered as two different functional genes or as different sites of the same functional gene cannot be decided. The frequency of 0·07 per cent is a value which is consistent with either alternative, and the important functional complementation test is not possible with this *A* locus in the present lack of knowledge of its action. But if the *A* locus is similar in *Coprinus* and in *Schizophyllum* which has two genes 4–10 per cent units apart, then two genes are indicated. It may be significant for the working of the incompatibility system that in all four species of higher fungi where recombination within the *A* and *B* loci has been tested on a sufficient scale, two sub-units or genes have been found.

Mutations affecting the *A* function were obtained in heterokaryons which had a common *A* allele. These were either changes at the *A* locus itself or at a gene suppressing the *A* function. All the mutants appeared to result in loss of function because monokaryons with these mutations produced spontaneously the clamps which are normally confined to dikaryons. A further analysis of the *A* locus using recombination and mutation should reveal further important details about its structure and function.

Prof. R. A. Raper (Harvard), who has been mainly responsible for the detailed analysis of the *A* and *B* loci in *Schizophyllum commune*, in his paper "An Enquiring Look at Tetrapolar Incompatibility", gave a penetrating and exhaustive review of the possible control systems which could be accommodated into the known facts about the *A*–*B* mating system in higher Basidiomycetes. Such a control system has to account for the high degree of specificity, and at the same time the great variation in the specific control. It also must be consistent with the genetic system, but as was pointed out, such a genetic system would have been subjected to exceptional selective pressures because of the unusual nature of the system, and it is possible that exceptional or even unknown gene action and interaction may be revealed by the system.

Three basic modes of biochemical control were considered: (1) an inhibitor system which is produced by like alleles to cause incompatibility; (2) an inhibitor which is present in the monokaryon, but which is removed by unlike *A* and *B* alleles to give a compatible dikaryon; (3) a complementary action between unlike alleles to elaborate an essential substance for the compatible dikaryon to become established. With our present knowledge of gene structure, function, interaction and complementation there are some difficulties with all three schemes, but Prof. Raper hoped that a solution might be forthcoming from a serological analysis which had already given promising results.

Prof. J. H. Burnett (Newcastle) described his results of surveying natural populations of several species of higher Basidiomycetes for their mating type *A* and *B* alleles. The survey included bipolar and tetrapolar species. The number of different alleles was large, but varied significantly between different groups. The genus *Nidularia* stands out from the rest by having a small number of alleles.

Fruit bodies sampled from the same tree and from the same clump revealed that different dikaryons were mixed together in a mosaic. Several examples of contiguous fruiting bodies were found to be genetically isolated from one another as shown by the failure of their spore colonies to mate. Mosaic cultures were reconstructed in artificial conditions, and it was concluded that the mycelium is not often a single ecological unit but a genetical mosaic.

The mosaic nature of the mycelium, together with the genetic sterility barriers between the components of a mosaic, may have its causative connexion. Genetically isolated components could only form a mosaic, but components not so isolated could fuse to give a dominant single dikaryon. But, like many aspects of higher fungi, whether this frequent isolation barrier has its cause in the unique mating system is not known.

D. Lewis

BARLEY AND BREWING

THE European Brewery Convention belongs wholly to the post-war period and, in retrospect, it is surprising that, prior to its inception, no organization existed for the regular international exchange of scientific information and experience in relation to malting and brewing. There were of course various journals of high repute, but the differences in standards, industrial methods and laboratory procedures from country to country were not widely appreciated. Consequently, valuable though many published investigations were, they tended more to describe particular experience than verifiable fact. With the present volume in mind*, it can be still more clearly seen that the selection of barleys and of malting methods even in a single country could scarcely have been done scientifically so long as the lack of properly documented experience made it impossible to co-ordinate the economic and material requirements of the farmer, maltster and brewer.

The tenth annual report reveals that these earlier deficiencies have been largely remedied by a degree of integration in international investigation never before achieved in this connexion. For example, it gives, mostly in tabular form, the results of trial comparative cultivations, often with relevant malting and brewing trials, of some 12 new varieties of barley the majority of which were grown under highly controlled conditions in 14 western European countries. The data extend far beyond the expected facts on such matters as yield, nitrogen-content, dormancy, grind characteristics of the malts and head retention of the final beers making up the series of part-reports, each under separate authorship. Thus they include numerous details of the lay-out of each trial, the nature of its location, agricultural conditions, field observations and meteorological data. The report is therefore a reference work rather than a book to be read cursorily. There can be no doubt that it reflects what is, in its way, an exceptionally important step to find improved varieties of what is the basic raw material of an unusually widespread industry.

It may seem strange to some that this effort is so disseminated when much of the work could apparently be carried out centrally. Actually, however, this type of inquiry is unexpectedly complicated because it involves comparison not only of barleys as such but also of the conditions under which they are grown and processed. Broadly, therefore, the question arises as to whether the differences between varieties can outweigh the differences arising from varying methods of treatment, for example, of malting method. The European Brewery Convention Barley Committee is in an unrivalled position to sponsor investigations of this kind, and its report has therefore a scientific value beyond that of a factual record of a unique but continuing international exercise.

A. H. COOK

* European Brewery Convention. *Rep. Barley Committee, 1959*. Pp. 170. (London: Institute of Brewing, 1960.)

ADMISSION TO UNIVERSITIES IN BRITAIN

THE third report of an *ad hoc* Committee on Procedure for Admission of Students to Universities, appointed by the Committee of Vice-Chancellors and Principals of Universities of the United Kingdom in January 1958, has now become available*. The Committee was set up to consider what steps need to be taken to reduce difficulties experienced by candidates for admission and by the schools. The report contains the findings of a working party established under the chairmanship of Dr. A. W. Chapman to report on the methods and techniques by which the multiplication of applications for admission and the consideration of candidates could be reduced, the kind of central organization involved and any changes of principle as regards relations between universities and candidate. The Committee has been forced to conclude that the time has come when universities must consider the establishment of a central organization and a central office in connexion with applications for admission, and it was this conclusion which led to the establishment of the working party. Further, having been satisfied as to the technical feasibility of such central arrangements, the committee also concluded that it must now make recommendations which would cause the universities as a matter of urgency to consider the rapid establishment of co-operative arrangements, and this is the whole burden of the report.

The working party quickly recognized that it would be essential to have some kind of central office with information about every candidate and every institution, but equally that a candidate must have liberty to apply to a reasonable number of institutions of his own choice, and that the choosing of their students must remain entirely a matter for the universities.

Three schemes were submitted by the working party for consideration by the *ad hoc* Committee. One scheme looks to the maintenance of the present system, and the central office would only act as an information centre, as a means of checking candidates stated priorities and acceptances of places, and, in so far as time permitted, as a clearing house. Acceptance of this scheme is not recommended.

The other two schemes provide for a central office, equipped with data-processing machines, to which each candidate would make his or her application, naming a limited, but reasonably generous, number of institutions, to which he or she wishes to apply. It would be the duty of the central office to distribute the applications to the institutions concerned, to act as the channel through which all offers, whether firm or provisional, or rejections are conveyed to the

* Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom. Third Report of an *ad hoc* Committee on Procedure for Admission of Students. Pp. v + 41. (London: Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom, 1961.) 2*s*. 6*d*.

candidate, to ensure that no other application remains in force once a candidate has accepted a firm offer, to provide a general clearing-up service operating from the earliest possible date in the admissions season, and to make full information to those who need it. Under the scheme preferred by the *ad hoc* Committee, though both are recommended to the consideration of the Committee of Vice-Chancellors and Principals, a candidate's applications would be released two or three at a time in an order chosen and specified by the candidate and a second pair of applications would ordinarily be released only after the results of the first pair had proved unacceptable. It provides that the selector must make a definite decision on an application within a given time-limit and can no longer wait until after his or her General Certificate of Education results before reaching a decision. Either scheme could be made effective for the intake of October 1964 if immediate steps were taken, and the Committee recommends the convening of a conference of representatives of the universities to consider the two recommended schemes and their application to the needs of the individual institutions.

Neither scheme need adversely affect the direct relation between candidate and institution. In the light of the discussion at the conference, the Committee of Vice-Chancellors and Principals would invite universities to agree to establish a standing advisory council, and to authorize the necessary steps to establish a central office, including a small executive committee which would act as its governing body and control its policy and operation. These proposals and recommendations are limited to universities in England and Wales other than Oxford and Cambridge, but it is hoped that the colleges of Oxford and Cambridge will also consider entering the scheme and that, even if they do not enter fully, they will at least arrange to complete their selections for admission by the end of December or not later than mid-January. The proposals also seem to be applicable without difficulty to the Scottish universities.

Figures appended to the report show that for the institutions covered 151,000 applications were lodged for 1960–61, against 134,000 for 1959–60, 121,000 for 1958–59 and 70,000 for 1955–56, and in all 22,650 students were admitted to first degree courses in October 1960, compared with 20,300 in October 1959. Of the applications, 14,000 were from overseas candidates. Except for technological courses, the number of applications increased substantially compared with the previous year, though the number admitted to such courses increased by about 12 per cent. There is a notable decrease in the number of vacant places, except in technology, and there seems to be no doubt that, at present, too few adequately qualified candidates are applying for courses in the technologies and especially in the classical engineering subjects. It would appear that the clearing-up houses, established in the summer of 1960, as recommended in the *ad hoc* Committee's second report, have already contributed to the decrease in the number of vacant places.

CÆSIUM-137 IN AIR, PRECIPITATION, DRINKING-WATER, MILK AND BEEF IN NORWAY DURING 1959 AND 1960

By T. HVINDEN and A. LILLEGRAVEN

Division of Physics, Norwegian Defence Research Establishment, Kjeller

CÆSIUM-137 in air, precipitation and milk has been regularly measured at Bergen, Røros and Lillestrøm. The results for January 1959–December 1960 are shown in Fig. 1 as mean values over periods of two months.

Cæsium-137 in beef-samples from the same districts has also been measured. Cæsium-137 in drinking-water has been regularly measured at several places.

The Bergen district is a mountainous coastal area, Røros district is a mountainous inland area and Lillestrøm district is a lowland, inland area. The locations are shown on the map in Fig. 1.

As shown in Fig. 1*B* the concentration of cæsium-137 in ground-level air is at nearly the same level at the three measuring sites, and the variations occur simultaneously. There is one maximum during May–June 1959 and another, but much lower, in May–June 1960. The yearly average values are:

District	1959	1960	
Bergen	0·020	0·0042	*μμc*, cæsium-137/m.³
Røros	0·019	0·0045	,,
Lillestrøm	0·019	0·0044	,,

The concentration of cæsium-137 per litre precipitation, shown in Fig. 1*C*, also varies in much the same way, but with a somewhat larger difference from site to site. The maximum concentrations in 1959 are found during the periods March–June, and so are the maximum concentrations in 1960. It appears, nevertheless, from Fig. 1*B* and 1*C* that the concentration of cæsium-137 per litre precipitation to a first approximation is proportional to the concentration in ground-level air.

The average cæsium-137 concentration in the total yearly precipitation is:

District	1959	1960	
Bergen	17	3·5	*μμc*, cæsium-137/l. precipitation
Røros	13	3·4	,, ,,
Lillestrøm	13	3·3	,, ,,

The rate of deposition of cæsium-137 fall-out, shown in Fig. 1*D*, depends on the amount of precipitation, which is very different from site to site. The maximum fall-out rates in 1959 are found during the periods March to August, and so are the maximum rates in 1960.

The yearly average rate of fall-out is:

District	1959	1960	
Bergen	67	13	*μμc*, cæsium-137/m.² per 24 hr.
Røros	10	4·1	,, ,,
Lillestrøm	29	8·9	,, ,,

Fig. 1*E*, showing cumulative cæsium-137 fall-out during January 1959–December 1960, reflects the difference in precipitation from site to site. The total yearly fall-out is:

District	1959	1960	
Bergen	24,300	4,800	*μμc*, cæsium-137/m.²
Røros	3,800	1,500	,,
Lillestrøm	10,600	3,300	,,

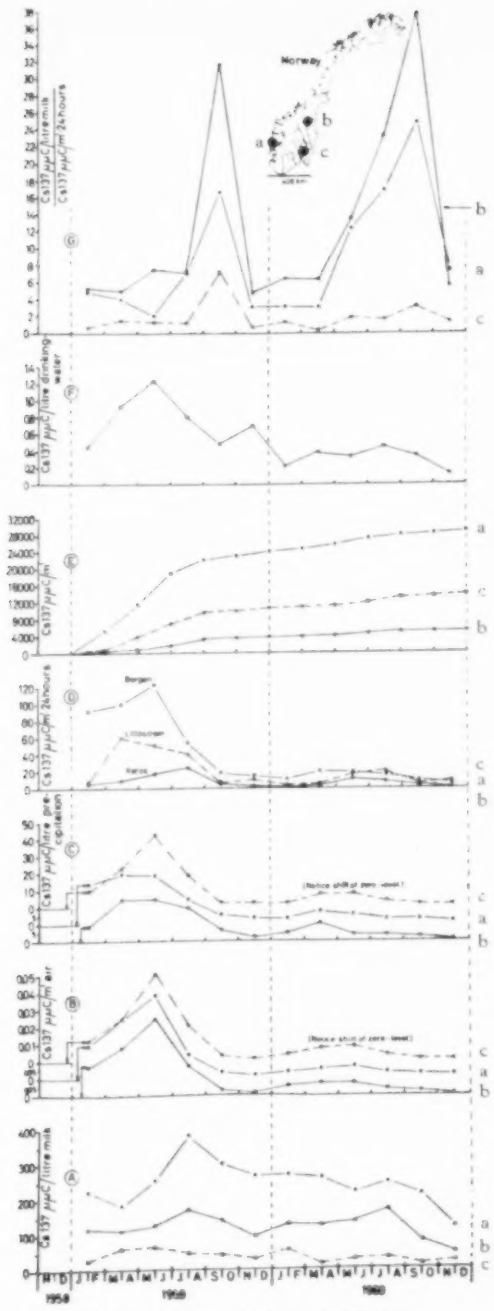

Fig. 1. (*a*) Bergen; (*b*) Røros; (*c*) Lillestrøm

It appears thus that the fall-out at Bergen is about 5 times higher than at Røros and about twice as high as at Lillestrøm.

The average concentration of cæsium-137 in drinking-water samples from 13 places in southern Norway, including Røros, is shown in Fig. 1*F*. The yearly average value is:

1959	1960	
0·8	0·3	$\mu\mu$c. cæsium-137/l. drinking-water

The average cæsium-137 concentration in drinking-water thus is only a few per cent of the average cæsium-137 concentration in precipitation.

The concentration of cæsium-137 in milk, shown in Fig. 1*A*, is also very different from site to site. The yearly average values are:

District	1959	1960	
Bergen	270	230	$\mu\mu$c. cæsium-137/l. milk
Røros	130	120	" "
Lillestrøm	47	29	" "

The concentration of cæsium-137 in milk at Bergen is about twice as high as at Røros and about 7 times higher than at Lillestrøm. The difference thus does not follow the difference in cæsium-137 fall-out.

At all three sites the concentration of cæsium-137 in milk shows a tendency to decrease towards the end of 1960.

The cæsium-137 concentration found in samples of beef during winter and early spring 1960 is:

Bergen	1,760 $\mu\mu$c. cæsium-137/Kgm. meat		(average of 2 samples)
Røros	590	" "	(average of 9 samples)
Lillestrøm	180	" "	(1 sample)

The variations in cæsium-137 concentrations in meat from district to district appear to follow nearly the same pattern as for milk.

The concentration of cæsium-137 in milk and meat corresponds to an intake by the cow of up to several thousand $\mu\mu$c. cæsium-137 per day. The intake may be through air inhaled, through drinking-water and through fodder. As the air inhaled by a cow is of the order of 200 m.³ per day, it is evident that the concentration of less than 0·1 $\mu\mu$c. cæsium/m.³ air does not contribute significantly to this intake. The drinking-water intake by a cow is of the order of 50 litres a day. The concentration in drinking-water of less than about 1 $\mu\mu$c. cæsium-137/l. therefore apparently does not represent any important contribution to the daily cæsium-137 intake by the cow. Even during summer time when the cow may be drinking water directly from pools, rivers, lakes, etc., with a somewhat higher concentration than ordinary drinking-water (but still lower than in precipitation), the intake of cæsium-137 by drinking-water does not amount to a large part of the total daily intake by the cow.

Apparently the main contribution to the intake of cæsium-137 by the cow is from cæsium-137 in grass, hay and possibly other fodder. The uptake of cæsium-137 by grass may so far have been mainly direct from rain and air, and less through soil and roots. It might be expected then that the concentration of cæsium-137 in grass and hay and therefore also in milk and meat to a first approximation would be proportional to the rate of cæsium-137 fall-out.

The ratio of cæsium-137/l. milk to cæsium-137/m.² per 24 hr. is shown in Fig. 1*G*. During the winter months November–April, the hay eaten by the cow is from the previous summer. The ratio shown in Fig. 1*G* for the winter months therefore is based on average cæsium-137 fall-out rate during the period May–August of the preceding summer. The average cæsium-137 fall-out rate during these months of 1958 was 47 $\mu\mu$c./m.² per 24 hr. at Bergen and 30 at Lillestrøm. The value at Røros has been calculated to be 23, based on rainfall data from Røros and average concentration per litre precipitation at Bergen and Lillestrøm during May–August 1958. The calculation adds an extra uncertainty to the two first points of the Røros curve in Fig. 1*G*.

It appears from Fig. 1*c* that the ratio of cæsium-137 in milk to cæsium-137 fall-out rate is different from site to site. The yearly average of the 2-monthly values is:

District	1959	1960	
Bergen	6·3	11	$\mu\mu$c. cæsium-137 l. milk
Roros	10	15	$\mu\mu$c. cæsium-137 m.$^{-2}$ 24 hr.
Lillestrom	2·1	1·6	

The difference in ratio may be taken to represent to a first approximation the difference in grazing-field qualities of the three districts, a low ratio corresponding to high grazing-field quality.

For all three districts the ratio-curve shows a maximum during the period September–October, both in 1959 and in 1960. It seems reasonable to relate this increase to the decreasing quality of the grazing fields in the late months of autumn, the slower growing rate of grass giving an increased cumulative effect in the cæsium-137 uptake by the plants.

At Bergen and Roros the ratio is somewhat higher in 1960 than in 1959. As Bergen had an abnormally dry summer in 1960, while Roros had a rather wet and cold summer, this may again be related to lower grazing-field quality during 1960.

On the other hand, the variations in the ratio of cæsium-137 in milk to cæsium-137 fall-out rate may depend on a number of other factors in addition to the grazing-field quality, such as variations in precipitation and fall-out amounts within each district, variations in feeding conditions including amount and type of additional fodder, delay between variation in cæsium-137 intake and resulting variation in cæsium-137 in milk, redistribution of fall-out, and also uncertainties in sampling and measurements.

NUCLEAR MATERIALS AND NUCLEAR CHANGE IN DIFFERENTIATION

By Prof. KENNETH MATHER, C.B.E., F.R.S.
Department of Genetics, University of Birmingham

IN a noteworthy series of experiments, Brink[1,2] has demonstrated that certain alleles at the *R* locus, affecting pigmentation in maize, are capable of showing two different kinds of change. One of these is the familiar phenomenon of mutation. It is sporadic, occurring in this case with frequencies of the order of 1 in 10^5; it is stepwise, in that the products of the mutation do not fall into a graded series; it is undirected; and it results in new alleles which are as stable as that from which they arose. The second type of change differs in all these respects. It is determinate, in that it occurs in 100 per cent of cases under certain conditions; it appears to be capable of giving rise to a graded series of products; it is directed in that a given allele always changes in the same way under the same conditions; and the changed alleles to which it gives rise are metastable, rather than stable, as attenuation of the effect has been observed. Brink terms this second type of change 'paramutation', and shows that the chromosome material on which it depends cannot be the same as that the changes of which appear as normal mutations. In other words, the *R* locus must be dual, containing orthochromatin, which provides the basic gene structure and which by its changes gives rise to true mutations, and parachromatin, which though not of the essence of gene structure nevertheless affects the expression of the gene's action and which by its changes gives rise to paramutations. Paramutation has been established as occurring at one further locus, at least, in maize, and there are indications if not full proof of it in other species[3].

Although at least partial reversion of the *R* paramutants has been observed in maize, the circumstances in which this occurs are not yet clear. In the fly *Sciara coprophila*, however, a similar type of change is to be inferred and the cycle is unambiguous. In the male flies meiosis is replaced by a division which results in one haploid set of chromosomes being eliminated, and this is always the set the male received from his father. The set originating from his mother is handed on to his progeny in which, if they are male, these chromosomes will now be eliminated. The chromosomes have thus changed from 'maternal' to 'paternal' behaviour following passage through the male. Should, however, they be passed by the male to a daughter (from which they are, of course, not eliminated) they will regain 'maternal' behaviour as will be made evident if this daughter in turn passes them on to a son[3].

Further evidence of the complete dependence of change in behaviour of the chromosomes on the sex of the fly through which they passed in the previous generation is supplied by the so-called *X* chromosomes. Each zygote, whatever the sex of the individual destined to develop from it, receives three *X*s, one from the mother and two from the father. The differences between the sexes become apparent at the fifth or sixth cleavage division in the somatic line, for in females one *X* and in males two *X*s are then eliminated from the nucleus. The *X*s to be eliminated are always of paternal origin. The sole remaining *X* of a male is thus maternal, but if it is passed on to a son in the next generation it will show paternal behaviour. One of the remaining *X*s of a female is, of course, maternal but the other is paternal. When passed on by the female to her offspring the two will behave alike as maternals, but if the offspring are male the chromosomes, while continuing to behave alike, will be changed to paternal behaviour as will be exemplified in offspring to which those males give rise in their turn. It has recently been shown that the *X*s owe these curious properties to heterochromatin at the centric end of the chromosome[4].

These changes in the chromosomes of *Sciara* are clearly comparable to paramutation (as indeed Brink points out) in three respects. They are directed; they are determinate, and indeed inevitable according to the sex of the fly which passes the chromosomes to its offspring; and they are metastable, being changed by passage through a fly of the opposite sex. The changes in chromosome behaviour are thus regular consequences of the processes of development and may in fact be described as parts of these processes. We cannot, however, be sure that they in their turn affect subsequent development, for we do not know that the fly would develop differently if a maternal *X* chromosome were to be eliminated instead of a

paternal. Indeed, the significance of this differential elimination of paternal chromosomes in *Sciara* is quite obscure.

Various other types of nuclear change are known to occur during development. Some of these, as, for example, the widespread phenomenon of endopolyploidy, are most readily understood not as adaptive changes playing a determinate part in development itself, but simply as the consequences of breakdown in the adjustment of the mechanism of nuclear division in cell-lineages which have come to the end of their history of cell multiplication[5,6]. No question of paramutation arises in this interpretation of endopolyploidy. In other types of change a kind of paramutation may be important. There is cytological evidence, some of it obtained by the use of tritium-labelled thymine[6,7], that the activity of the genes in *Drosophila* changes, and changes differentially, during development. The observations further suggest that these changes must be associated characteristically with the different tissues so that they are determined by the state of the cells in the tissues and indeed are inevitable under the condition of the tissue, just as the chromosome changes of *Sciara* are determined by and inevitable in flies of a given sex. Similar changes in gene action are indicated by King and Briggs's observations[8] on the nuclei of developing frog embryos. I have earlier suggested[9] that these changes are to be interpreted not as changes in the basic content of the genes of the nucleus, but as brought about by the depletion from or accretion to the chromosomes of what I called 'ancillary materials', which, while not of the genes, affect the action of the genes—an interpretation bringing in the same type of change as that which Brink now terms paramutation, with his parachromatin corresponding to my ancillary materials.

In all these cases change is consequent on development, but in none of them is there clear evidence (as opposed to arguable presumption) that the change plays a positive and constructive part in determining the course of future development. The evidence from King and Briggs's frogs is of nuclei which have lost the capacity to sustain the full range of development when put back into the cytoplasm of a fertilized egg. This could indicate (though it does not necessarily do so) no more than a characteristic loss of gene function, just as the cytoplasmic changes associated with certain aspects of differentiation in the fungus *Aspergillus nidulans* are losses of certain capacities rather than constructive gains[8]. There would seem, however, to be no reason in principle why changes of a paramutational type arising during development should not actively and constructively determine the further developmental history of the cells and tissues in which they occur. It is especially tempting to attribute to paramutation the stability which is reached in cells at the end-point of their differentiation. The mechanical control which the chromosome system exercises over nuclear genes gives to these a regularity of behaviour and precision of balance which the cytoplasm could not be expected to emulate, and the evidence from maize and *Sciara* shows the parachromatin or ancillary materials to behave as regularly and be transmitted as precisely as the genes themselves, except, of course, when they are undergoing their determinate changes from one metastable state to another.

Clearly, therefore, paramutational types of change in the chromosomes could play an important part in development. They could not, however, of themselves offer any interpretation of differentiation, for even if we attribute alteration in the behaviour of a cell to such directed and determinate change in its chromosomes, we are still not enabled thereby to see why two sister cells, derived by division of a single mother cell, follow different courses of development. If the parachromatin or ancillary materials share with the other and fully permanent materials of the chromosome the property of equal division in cell reproduction they can no more account of themselves for sister cells following different paths than can those other chromosome materials. So we must still return to the cytoplasm if we are to understand differentiation. The divergences of differentiation must spring basically from differences in the cytoplasmic materials[8,11] even though secondarily it may involve nuclear differences, including paramutational changes, arising as responses to the initial cytoplasmic differences.

We are thus led to inquire whether changes in the cytoplasm can bring about changes in the nucleus, and more particularly paramutational changes. Changes of gross nuclear behaviour during differentiation are, of course, well known and some of them are demonstrably responses to cytoplasmic differences, as, for example, the polymitotic behaviour of nuclei in a mutant strain of maize and the differences in rates of condensation between generative and vegetative nuclei in pollen grains[5,11]. It is known, too, that in bacteria material can exist at times as particles in the cytoplasm and at others as an integral part of the chromosomes, the transition from one state to the other being promoted by specifiable conditions[12]. Furthermore, it is difficult to avoid the conclusion that both Brink's paramutations in maize and the similar changes of chromosomes in *Sciara* involve something outside the chromosomes as an intermediary. In maize, paramutation of the allele on one chromosome is dependent on the presence of an allele not in the same chromosome but in its homologue, so that the paramutagenic action must be exerted extra-chromosomally. In this case the effect may be exerted through the nucleoplasm, as opposed to the extra-nuclear cytoplasm. With the changes of chromosome behaviour in *Sciara* the cytoplasm is more directly implicated since the sex of an individual, and therefore the type of behaviour which its chromosomes will come to assume and express in its offspring, is dependent not on its own but on its mother's genotype and thus on the presence of genes which it itself does not always possess. The cytoplasm would therefore appear to be the intermediary, being conditioned by the genotype of the mother but exerting its effect, of determining the state of the chromosomes, in the offspring. Thus paramutation, like any other nuclear change in development, must be due directly to an action of the cytoplasm (or at least extra-chromosomal plasm) on the nuclear materials and only indirectly on the genes which acted to change and mould that cytoplasm in the first place. The significance of paramutation in development would thus be that it fixed, so to speak, the initially cytoplasmic changes, and gave to them a precision in cell heredity that purely cytoplasmic transmission could not guarantee. In this way paramutational changes, depending on the presence and changes of parachromatin or ancillary materials in the chromosomes, could be of great significance in development. But in differentiation

they could have only a derived significance springing from and dependent on the reflexion—one might almost say crystallization—by paramutation of primary changes in the cytoplasm to which indeed differentiation must still ultimately be referred.

It is worth noting, too, that if the normal cytoplasmic progression of differentiation is reflected at least partly in a progression of materials in the chromosomes, these chromosome materials, like the cytoplasm, must either remain unchanged in the cell lineages from which gametes are derived or their progression must come full circle. Otherwise the individuals of the next generation would not start off their development from the same point as did the parents. If developmental change occurs at all in the germ-line, there must be a parachromatinic re-standardization—a clean-up of the ancillary materials in the chromosomes—just as there is of the cytoplasm in the sexual cycle of *Aspergillus glaucus*[10]. This re-standardization is not indeed observed in paramutation at the *R* locus in maize; but here the changes are not characteristic components of development, and indeed if there had been a re-standardization Brink could never have recognized or investigated the phenomena.

Clearly there is need for further studies of paramutation in its relation to the cytoplasm in development and differentiation. This relation may also be of importance in another connexion, for if cytoplasmic change can bring about paramutational alterations of the chromosomes it is possible that external intervention may, through its effects on the cytoplasm, also bring about directed changes of the hereditary materials. The remarkable changes observed by Durrant[12] may be of this kind. He 'conditioned' flax plants by growing them in artificially fertilized soils and found that the plants transmitted the change type not only to the offspring they gave by self-fertilization but also to their crossed progeny, the transmission being equal through pollen and egg. The changes were determinate and specific yet apparently nuclear in transmission: they are capable of obvious interpretation in terms of ancillary materials or paramutation as I have been discussing it. Other alterations of a similar kind can be interpreted in the same way, as may be wider observations of cytoplasmic effects which somehow seem to become attached in transmission to the nucleus (see Roper[13]). In these cases, however, the interpretation is less clear and must remain so until the results of further experiments become available.

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THE IONIC CHARACTER OF CHEMICAL BONDS

By E. MOOSER and W. B. PEARSON

Division of Pure Physics, National Research Council, Ottawa, Canada

IN recent years various attempts have been made to determine the effective charges on the atoms of semiconducting compounds from a discussion of the chemical bonding in these materials. While these attempts have not succeeded in reaching their goal, they have led to considerable confusion about the partial ionic character of covalent bonds[1]. In an effort to clear up this confusion we have had many vigorous discussions with our colleagues, and since we believe that the conclusions drawn from these discussions might be of interest to other scientists, we would like to summarize them here.

One of the causes of confusion is the synonymous use of the words 'covalent' and 'homopolar', a mistake which is readily understandable since the simplest examples of covalent bonding—the bonds in the hydrogen molecule and in diamond—are also examples of homopolar bonding, that is, bonding between 'uncharged' atoms. However, the definition of a covalent bond as first given by Langmuir[2] and as adopted by Pauling[3] states that such a bond arises from the 'equal sharing of two electrons' between the two bonded atoms, and thus makes no reference at all to the effective charges on the atoms.

The two distinctly different meanings at present attributed to the term 'ionicity' or 'ionic character of a bond' present a second more serious source of confusion. Lest we contribute further to the confusion we will therefore, in the following, distinguish between an 'effective' and a 'formal' bond ionicity.

Discussing the 'effective' bond ionicity first, we note that an ionic bond results "from the Coulomb attraction of the excess electric charges of oppositely charged ions"[4]. It readily follows from this definition that if two neighbouring atoms (ions) in a molecule or solid carry opposite charges, then the bond between them will have some effective ionic character. Unfortunately, it is difficult to define an unequivocal scale of effective bond ionicity, because whereas zero ionic character obviously corresponds to zero charges on the ligands, it is sometimes not immediately clear to which degree of ionization of the ligands 100 per cent effective bond ionicity has to be ascribed. However, by convention a bond between two atoms is normally called 100 per cent ionic if the atoms are ionized to the extent that at least one of them acquires a noble gas shell. This convention allows us to call a compound purely ionic if all its bonds have 100 per cent effective ionic character. Moreover, because an ion with a noble gas shell cannot form any covalent bonds, the convention assures that a bond with 100 per cent ionic character cannot have a covalent component.

It follows from the above discussion that the percentage i_e of effective ionic character of the bond between two atoms A and B is closely related to the

'effective charges' q_A and q_B on these atoms. Indeed, if q_{0A} and q_{0B} are the charges which the two atoms would carry if the bond between them were completely ionic, then:

$$i_e = \frac{q_A}{q_{0A}} \times 100 = \frac{q_B}{q_{0B}} \times 100 \qquad (1)$$

We note that the definition of the effective ionic character of a bond as given by (1) is identical with that used by Pauling[3] in discussing the relationship between bond ionicity and dipole moment μ of the hydrogen halogenide molecules (see also Hannay and Smyth[4]). Indeed, if r_0 is the equilibrium distance between the two atoms of such a molecule, we find for the effective charges $q_A = -q_B = q$ on the atoms:

$$q = \mu / r_0 \qquad (2)$$

and hence for the effective bond ionicity:

$$i_e = \frac{\mu}{r_0 q_{0A}} \times 100 = -\frac{\mu}{r_0 q_{0B}} \times 100 = \frac{\mu}{r_0 e} \times 100 \qquad (3)$$

where e is the electronic charge.

Contrary to the effective bond ionicity, the 'formal bond ionicity' is not related to any quantity such as the effective charge, which is at least in principle measurable. (For diatomic molecules the effective charge is defined by (2) and hence can readily be determined experimentally. Unfortunately, this definition cannot be extended to include complex molecules and solids. Nevertheless, any discussion of effective bond ionicities implies that effective charges can, at least in principle, be measured, because the ionic bond itself is, after all, defined in terms of such charges.)

The formal bond ionicity is a purely theoretical concept, and its numerical value depends on the approximation used in describing a bond and not on the actual properties of this bond.

Because no method is available for solving many-electron problems accurately, it is often assumed[3,5] that the bonds in molecules or solids can, with sufficient accuracy, be described as resulting from the resonance of these molecules or solids among different valence structures. Let us discuss briefly a diatomic molecule AB the components of which have one valence electron each (monovalent atoms). Chemical and physical intuition tells us that it is reasonable in this case to consider the following valence structures:

$$A : B \qquad A^+B^- \qquad A^-B^+$$

Corresponding to equal sharing of the valence electrons by the two partners, the first structure is called 'covalent'. For obvious reasons, the other two structures are both called ionic.

Let $\Psi_{A:B}$, $\Psi_{A^+B^-}$ and $\Psi_{A^-B^+}$ be three properly chosen two-electron wave-functions corresponding to the three valence structures. With these functions we form the linear combination:

$$\Psi = a\Psi_{A:B} + b\Psi_{A^+B^-} + c\Psi_{A^-B^+} \qquad (4)$$

and determine the coefficients b/a and c/a such as to minimize the integral:

$$E = \frac{\int \Psi^* H \Psi \mathrm{d}\tau}{\int \Psi^* \Psi \mathrm{d}\tau} \qquad (5)$$

Substituting these coefficients in (4), we obtain the best wave-function which can be constructed by combining linearly $\Psi_{A:B}$, $\Psi_{A^+B^-}$ and $\Psi_{A^-B^+}$. The formal ionic character of the bond $A - B$ is then determined by the extent (measured by the coefficients b/a and c/a) to which the structures A^+B^- and A^-B^+ contribute to Ψ.

It is obvious from this discussion that the formal ionic character of a bond is defined only with respect to the particular approximation used in describing the bond. Thus if, for example, the electronegativity of atom B is much larger than that of atom A, it is sufficient to consider only the first two of the above valence structures, and (4) takes the form:

$$\Psi = a\Psi_{A:B} + b\Psi_{A^+B^-} \qquad (6)$$

The corresponding percentage i_f of formal ionic character of the bond then is given by:

$$i_f = \frac{(b/a)^2}{1 + (b/a)^2} \times 100 \qquad (7)$$

The two valence structures considered here in describing the bond in a molecule of monovalent atoms are obviously the same as those defining the scale of effective bond ionicity in such a molecule. It is permissible therefore to put:

$$i_f = i_e \qquad (8)$$

and one can in this case determine the only free parameter in (6), namely b/a, from the experimental value of i_e, thereby avoiding the cumbersome process of minimizing (5).

Equation (8) is perhaps the cause of all the confusion about bond ionicities. We would like to emphasize, therefore, that in spite of the conditional validity of (8), formal and effective bond ionicities are not identical, and one does well to distinguish carefully between them, particularly when discussing solids. Moreover, (8) should never be interpreted as implying that the effective ionic character of a bond can be derived from a formal bond ionicity. Indeed, if the effective ionicity of a bond is not known, the value of any formal ionicity attributed to this bond is always arbitrary, because it is necessarily based on arbitrary mixing of arbitrary, if plausible, valence structures.

To demonstrate the confusion which can arise from the indiscriminate use of the term 'bond ionicity', let us briefly dwell on a fallacious but often repeated discussion of the bonding in semiconductors of the zincblende type. This discussion, which has perhaps been instigated by Pauling's somewhat misleading account of the bonding in AlP (ref. 8), will here be given for zinc blende itself. The tetrahedral bonds in this compound are said to arise from resonance among the following two valence structures:

$$Zn^0S^0 \qquad Zn^{2+}S^{2-}$$

The first of these is referred to as the 'extreme covalent' structure, because it leaves each of the components with four valence electrons which can be shared in the formation of the maximum number of four tetrahedral bonds. The second structure is called 100 per cent ionic since it corresponds to a noble-gas configuration on both the zinc and the sulphur ions. These valence structures are taken to define the scale of bond ionicity (one is left guessing whether it is formal or effective ionicity), so that the bonds in the hypothetical 'neutral-bonded' Zn^0S^0 obtain 50 per cent ionic character[1]. Since sulphur is more electronegative than zinc, it is then concluded that in the crystal each sulphur carries some negative and each zinc the same amount of positive charge. Hence, the argument goes on, the bonds in ZnS are more than 50 per cent ionic. Such

a statement is very misleading indeed, and matters are only made worse if, as has been done, one goes a step further and calls ZnS a compound with more than 50 per cent ionic character.

We should, perhaps, recall here that the generally accepted definition of the covalent bond as given earlier leaves the effective charges on the ligands unspecified. To define the zero of effective bond ionicity by an arbitrary valence structure such as $Zn^{2-}S^{2+}$ is therefore meaningless, even though one might choose to call the structure 'extreme covalent'. Finally, we should like to repeat that out of any discussion of formal bond ionicities one can never obtain more information than was originally put in. In particular, any attempts such as have been made to determine effective charges from formal bond ionicities are bound to fail.

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EFFECT OF TEMPERATURE ON ADHESION TO GLASS AND HISTOGENETIC COHESION OF DISSOCIATED CELLS

By Prof. A. MOSCONA

Department of Zoology, University of Chicago

ONE of the chief attributes of metazoan cells is their ability to cohere and interact mutually into integrated, multicellular systems. Though the mechanisms of cell cohesion and the role of cell contact in development and in tissue function have had a long history of interest and speculation, recent reviews of these problems[1] clearly underscore the paucity of basic information on various important aspects. Among the theoretically and practically more obvious and pressing questions is that of the effects of temperature on the capacity of cells to adhere to various substrates and to each other. Though such information would seem prerequisite for a systematic inquiry into the mechanisms of adhesion and interaction of cells, the point has been surprisingly little studied. The methodology of dissociation and aggregation of embryonic cells[2] affords a direct approach to these problems: in connexion with present work on tissue-synthesis *in vitro* from dissociated cells[3,4], the question of temperature and cell adhesion was examined and some of the findings are reported here briefly.

Chemically dissociated cells[2,4] from neural-retina, liver and kidney (mesonephros) of 7-day chick embryos were used throughout this work. The cells were suspended in a standard culture medium (Eagle's basal medium with 1 per cent glutamine, plus 10 per cent horse serum, 2 per cent fresh embryo extract in Tyrode's solution, and 50 γ/c.c. penicillin–streptomycin).

Adhesion to glass. 2 c.c. aliquots of cell suspension (10^6 cells/ml.) were distributed into flat, 15-ml. T-flasks, filled with 5 per cent air containing carbon dioxide and sealed. Groups of flasks were kept at 38°, 30°, 25° and 15° C. The cells settled rapidly on the floor of the flasks and were not disturbed for 24 hr. They were then examined and the number of attached and unattached cells determined.

The three kinds of cell populations tested gave essentially similar results. At 38° C., 85–90 per cent of cells adhered firmly to the glass and were not dislodged by gentle flushing. The individual attached cells were flattened or rounded; others were in small spheroid clusters also stably attached to the glass. At 30°, about 60 per cent of the cells were firmly attached; at 25°, less than 40 per cent adhered stably. At 15°, cells did not adhere: even when left for 72 hr. in continuous contact with the floor of the flasks there was no attachment. When cultures from sub-optimal temperatures were transferred to 38°, there was rapid and abundant attachment of cells to the flask. It appears, therefore, that in the present case adhesion of cells to glass depended on temperature-sensitive processes which were completely, but reversibly, inhibited at 15° C. Interpretations of the mechanism of cell adhesion in such and similar systems must, therefore, account for the temperature-dependence of this cellular activity.

Histogenetic cohesion. To find out whether cohesion and histogenetic bonding of dissociated cells also were dependent on temperature, a procedure was sought which would: (1) render it possible to bring discrete cells rapidly into contact, independently of their capacity for locomotion, and without forceful packing (as by centrifugation); (2) reveal differences in stability and effectiveness of intercellular contacts under diverse testing conditions; (3) yield consistent results in a form amenable to quantitation. These requirements are adequately met by the 'rotation-mediated cell aggregation' procedure, described in detail elsewhere[4]. Erlenmeyer flasks with cell suspension are rotated on a gyratory shaker with a $\frac{3}{4}$-in. diameter motion. Due to the spinning flow of the liquid, all the cells are rapidly concentrated in the middle of the vortex and, if capable of cohesion, become soon bound into compact aggregates in which they construct tissue. The size distribution of aggregates thus formed reflects an equilibrium between cell cohesiveness under the given conditions, and the shearing forces of the system: the lesser the capacity of cells to cohere (or the fewer the number of cohesive cells, or the stronger the shearing forces), the smaller the resulting aggregates. All experimental parameters in this system are rigorously controllable, and under standard conditions diagnostically consistent 'aggregation patterns' are obtained, characteristic for diverse cellular and environmental situations.

In the present case, aggregation patterns produced at 38° C. by suspensions of 7-day embryonic chick cells (as above) served as a basis for testing the effects of lower temperatures on cell cohesion.

3-ml. aliquots of cell suspension (3×10^5 cells/ml.) were dispensed into 25-ml. Erlenmeyer flasks and rotated at 70 r.p.m. at 38°, 30°, 25° and 15° C. After 24 hr., size distribution of aggregates and number of free cells in each culture were determined. At 30° and 25° there was a significant and consistent decrease in size of aggregates of all cell types tested, illustrated for neural-retina cells in Figs. 1 and 2. This was accompanied by an increase in number of free cells. At 15° the cells did not cohere at all, and aggregates were not formed; even when maintained in continuous contact for 72 hr. at this temperature, the cells remained entirely discrete. Transferred to 38° C. such cells cohered into histogenetically effective aggregates. It should be pointed out that 15° C. is not the starting temperature for complete inhibition of cell cohesion; more recent results indicate that neural-retina cells may not cohere at about 18° C. and that sensitivity in this respect varies with cell type, state and culture medium.

The foregoing results reveal a clear correlation between temperature and ability of freshly dissociated avian embryonic cells to adhere to glass or to cohere mutually. The finding that at 15° C. cells are completely unable to become attached, though in prolonged and continuous contact, appears particularly useful towards further study of the mechanism of cell adhesion. It indicates that simple reactions between divalent cations (calcium, magnesium), or other first-order physico-chemical effects cannot be exclusively responsible for cell adhesion, as such reactions are unlikely to be persistently inhibited at 15° C. It also suggests that the exogenous molecules prerequisite for normal adhesion of cells (divalent cations, serum proteins[3,5]) provide only parts of the actual mechanism or contribute otherwise partially to its effective function, and that endogenous thermo-sensitive processes may have a highly important, perhaps primary, role in this cellular activity[6]. It is therefore proposed that cell adhesion may depend on metabolic sequences and closely reflect the metabolic economy of the cells; therefore, that it is not merely a result of coupling between

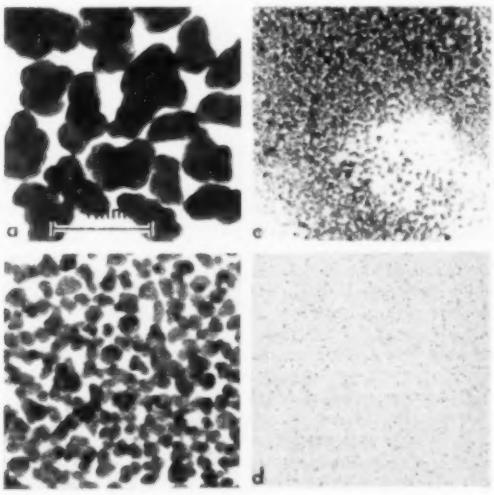

Fig. 1. 24-hr. aggregates of dissociated neural-retina cells (7-day chick embryo) formed in rotating cultures (70 r.p.m.) at 38° (*a*), 30° (*b*); 25° (*c*) and 15° C. (*d*); the cells remained separate

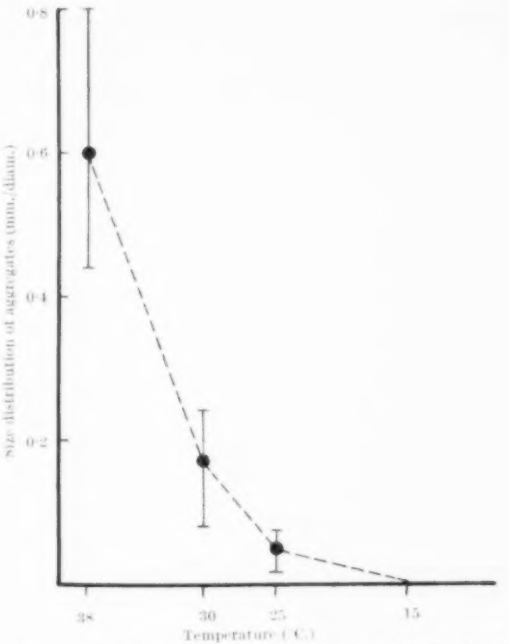

Fig. 2. Effect of temperature on size distribution of aggregates of dissociated neural-retina cells

stable surfaces, but also a function of the synthetic activities of cells. Assuming this, cell adhesiveness would be expected to vary with different functional states of cells; evidence to this effect is forthcoming, and can also be inferred from various, indirectly related, data in the literature.

The present findings appear to fit in with the working assumption[3] that (1) adhesion and histogenetic bonding of cells involve the production and organization between cells of mucoprotein-containing extracellular materials, the formation or effective function of which requires divalent cations and certain large molecules in the cellular environment; (2) rate of formation and properties of extracellular materials vary with type, age, metabolic pattern and treatment of cells; at low temperatures synthesis of extracellular materials is impaired resulting in failure of dissociated cells to become effectively attached.

This work was supported by grants from the National Cancer Institute, U.S. Public Health Service (C-4274), and from the Dr. Wallace C. and Clara A. Abbott Fund of the University of Chicago.

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MAGNETIC SUSCEPTIBILITY OF NORMAL LIVER AND TRANSPLANTABLE HEPATOMA TISSUE

By FRANK E. SENFTLE
United States Geological Survey, Washington, D.C.

AND

ARTHUR THORPE
Howard University, Washington, D.C.

IN 1948, Barnothy[1] found that young female mice, when placed in a $(3\text{-}6) \times 10^3$ oersteds magnetic field, underwent a temporary retardation of growth. The magnetic field apparently hindered mitosis. Barnothy *et al.*[2] reported a significant drop in the segmented leukocyte count in mice while confined in a magnetic field, whereas when they were removed from the field the count increased to peak values more than 100 per cent higher than the normal value. From these and other related experiments[3–7] with biological materials in magnetic fields, it can be inferred that a magnetic field may have a significant effect on growth of cancer cells. In support of this thesis, Barnothy reports[8] that at the University of Budapest he obtained good recovery results on albino mice inoculated with *Y* 2146 adenocarcinoma. Of the animals placed in an inhomogeneous magnetic field of 3,000–3,500 oersteds, there was loss of tumour in 5 and complete recovery in 4 cases out of 6, whereas there was 100 per cent mortality in the control animals. It has thus become increasingly clear that as a next step a more fundamental study of the magnetic properties of cancer and normal cells should be made. A comparative study was therefore undertaken of the magnetic susceptibilities of both types of cells. The results in this article indicate that the magnetic properties of transplanted hepatoma and normal liver tissue are different, and that the difference is probably associated with the way in which the water is held by the respective cells.

As an exploratory experiment, measurements were made on the normal and host tissue from the same organ (human larynx) which had been preserved in formaldehyde. The specimens were thoroughly dried, and several milligrams of tissue were removed with a glass knife for each measurement. No steel instruments were used in order to avoid unnecessary ferromagnetic contamination. The average magnetic susceptibility at room temperature of the tumour and normal tissue from this organ was $(-0{\cdot}61 \pm 0{\cdot}008) \times 10^{-6}$ e.m.u./gm. and $(-0{\cdot}57 \pm 0{\cdot}007) \times 10^{-6}$ e.m.u./gm. respectively. The difference is considered significant as it is several times the experimental error.

In view of these results, two series of controlled experiments were performed with rats. By means of trocar inoculation, a transplantable hepatoma was allowed to develop in some of the rats for 4–8 weeks. The tumour-bearing and control animals were then killed and the liver and transplanted tumour tissue removed. As soon as the tissue was removed from an animal, it was quick-frozen in liquid nitrogen to prevent any serious deterioration of the cells and remained there until the measurements could be made. The specimens were then removed from the liquid nitrogen and a small sample ($\approx$10 mgm.) was removed by cracking the frozen organ in a porcelain mortar. The entire sample preparation was performed in a refrigerated room held to within a few degrees of 263° K. so as to preclude any thawing of the specimen.

Although a steel scalpel was used to remove the tissue from the animal, non-ferromagnetic instruments were used thereafter in handling the samples to prevent contamination. By selecting a sample of frozen tissue from below the surface of the specimen ferromagnetic contamination could be minimized. However, to ensure further against this effect, each sample was measured at several magnetic field strengths. The apparent magnetic susceptibilities were then plotted against the reciprocal field (see Fig. 1) at each field strength after the manner of Owen[9] and Honda[8]. As ferromagnetism is dependent on field, the ordinal intercept is thus the susceptibility corrected for ferromagnetic impurity.

The magnetic susceptibility measurements were made by a modified Faraday method using a sensitive quartz helical spring balance described elsewhere[9]. The balance was placed in the same refrigerated room described above. Considerable difficulty was encountered in making the measurements due to the change in mass caused by evaporation of moisture at certain temperatures. Because the moisture content of the cold room was reasonably constant, little difficulty was experienced in making the measurements at 263° K. in air. At lower temperatures, however, carbon dioxide and some of the rare gases will condense out of the air, and hence helium had to be used as a heat transfer gas. As the helium was very dry, the sample tended to lose water. For each of the measurements in helium at temperatures between 170° K. and 263° K., the mass of the sample was remeasured using the quartz helix without a magnetic field, that is, as an analytical balance. In this way, a correction for loss of moisture could easily be made. At temperatures below 170° K., the vapour pressure of ice is so low that the change in mass due to loss of moisture is negligible.

In the first experimental series, two rats of the $A \times C$ strain were used for the tests. The tumour was allowed to grow for four weeks after inoculation in one rat, the other was used as a control. At the end of this period, the animals were lightly anæsthetized, and the liver and tumour tissue removed and

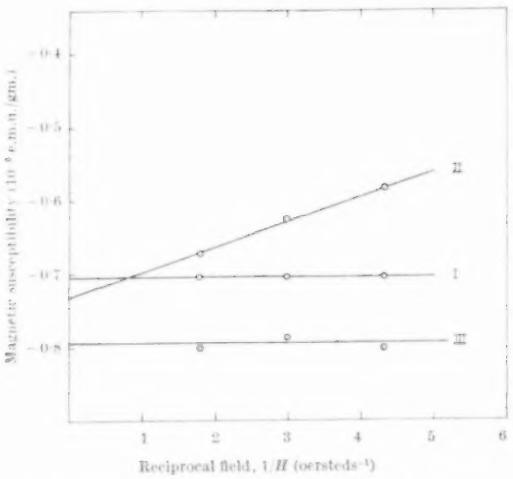

Fig. 1. Magnetic susceptibility of normal liver tissue from control animal (I) and liver (II) and transplanted hepatoma tissue (III) from tumour-bearing rat as a function of the reciprocal magnetic field

frozen. After loading a small sample on the balance, helium was admitted to the system and the temperature immediately dropped to liquid nitrogen temperature. By using this technique on each specimen of this series, a minimum amount of water was lost by evaporation. Re-measurement at room temperature in moist air allowed a correction to be made for this small loss.

All the measurements of this series were made at liquid-nitrogen temperature for another reason. If the cancer cells contained an abnormal amount of some paramagnetic impurity as, for example, some free radical, one would expect a paramagnetic component in addition to the basic diamagnetism of the cells. As the positive magnetic susceptibility of many paramagnetic substances increases as the temperature is lowered, it was thought worth while to take advantage of this enhancement if it existed in these specimens.

The susceptibilities plotted against the reciprocal field are shown in Fig. 1. The susceptibilities corrected for ferromagnetism (ordinal intercept values) of all the specimens are diamagnetic, the tumour tissue being more diamagnetic than the normal tissue as it was in the previous measurements. Although the results of the previous experiment on larynx tissue should not be compared too closely with these because of the differences in kinds of tissue, the pattern of the results is similar. The fact that the susceptibilities at the lower temperature are more diamagnetic would seem to suggest that the major differences between the normal and tumour tissue are not due to the presence of a paramagnetic substance.

The dependence on field shown in Fig. 1 for the liver from the tumour-bearing host rat indicates ferromagnetic impurity. At first this was thought to be a significant property of the tissue, but subsequent repeated measurements on samples of liver from other tumour-bearing host rats lead us to believe that this impurity was probably contamination.

To substantiate the results of this experiment, tissue from three more rats with transplanted hepatoma No. 3683 and three normal control animals was measured. To obtain a better temperature comparison with the first series, the measurements in this second series were first made at 263° K. in air. The results shown in Table 1 again show the same pattern, but in this instance are comparable with those in Fig. 1. The diamagnetic susceptibilities are lower, and the differences between the susceptibilities of the two kinds of tissue are smaller.

Table 1. Magnetic Susceptibility of Tumour and Normal Tissue of Rats*

Sample No.	Magnetic susceptibility (in 10^{-6} e.m.u./gm.)	
Transplanted hepatoma Morris No. 3683		
II-1	− 0·680	
II-2*a*	− 0·695	
II-2*b*	− 0·675	− 0·688 ± 0·0046
II-3*a*	− 0·691	
II-3*b*	− 0·700	
Liver tissue from tumour-bearing rat		
II-1	− 0·668	
II-2	− 0·671	− 0·670 ± 0·0012
II-3	− 0·672	
Liver from normal control animals		
II-4	− 0·629	
II-5	− 0·649	− 0·637 ± 0·0059
II-6	− 0·634	

* All the results have been corrected for ferromagnetic impurity, and have been taken at 263° K.

To explain these results better, the susceptibilities of duplicate samples of the same specimens listed in Table 1 were determined as a function of temperature from 77° K. to 263° K. No change was observed in the force on the sample as the temperature of the system was dropped from 263° K. to about 160° K. Therefore, independence of temperature was assumed in this region. Below 160° K., the force on the sample began to change and more measurements were made down to 77° K.

The results shown in Fig. 2 throw considerable light on the problem. The results for the tissue from the tumorous animals resemble a change-of-state curve exhibited by many substances[10]. As the change in the susceptibility at about 130–140° K. is so pronounced, it is not likely that it could be caused by a substance present in trace amounts. Due to high concentration in cell tissue, water or ice must be suspected. The magnetic susceptibility of ice is not well known in this temperature-range, so a series of measurements on ice was made following the same general procedure as outlined here. The

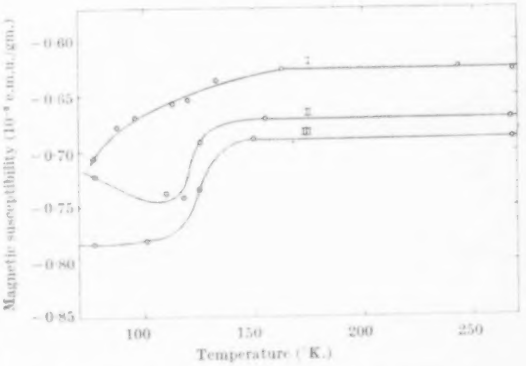

Fig. 2. Magnetic susceptibility as a function of temperature of normal liver tissue (I) and liver (II) and transplanted hepatoma No. 3683 tissue (III) from tumour-bearing rat

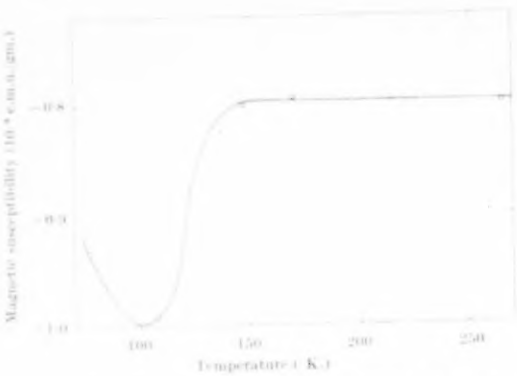

Fig. 3. Magnetic susceptibility of ice from distilled water as a function of temperature

results are shown in Fig. 3. The shape of the curve is so similar to those of the hepatoma and liver of the tumour-bearing host that one is led to conclude that the general feature of these curves is primarily due to the magnetic properties of ice rather than of the tissue itself. The break in the curve at about 130–140° K. is undoubtedly due to the change in state. Ice changes from hexagonal to the low-temperature cubic form at some temperature near 173° K.[11]. However, below 133° K., Lisgarten and Blackman[12] have shown that the X-ray diffraction pattern becomes diffuse. It is probably a change in crystal size or strain which accounts for the diffuse X-ray pattern and also the increase in diamagnetism of ice at about the same temperature.

To substantiate further the fact that changes in the magnetic properties of water are the chief reason for the characteristic form of the magnetic susceptibility curve of tumour tissue, an attempt was made to remove the water in the tumour cells by evacuation at 263° K. The residual tissue, however, was so spongy that it was extremely difficult to get enough material for the measurement in the homogeneous part of the magnetic field of the magnets. As an alternative, the effects of water in egg whites was measured for comparison. Curve I of Fig. 4 shows the change in the magnetic susceptibility of fresh egg white as a function of temperature. The results are similar to that of pure water and also the tumour tissue. The egg white was then slowly evacuated for 48 hr. at room temperature, and a 14·7-mgm. sample was loaded on the magnetic balance. The balance chamber was then further evacuated for an additional 18 hr. until constant weight was achieved. The subsequent susceptibility measurements (curve II, Fig. 4) show the absence of the magnetic properties of water. From these experiments it is reasonable to assume that the general features of the susceptibility curves of the tumour tissue are essentially due to the effects of water.

As water is diamagnetic ($-0{\cdot}7\times10^{-6}$ e.m.u./gm. at 273° K.) and as livers of tumour-bearing animals are known to contain more water than normal liver tissue[13–15], the more diamagnetic character of the liver tissue from the tumour-bearing host compared with normal tissue is reasonable. Apparently, the same is true of hepatoma, although some tumours are known to contain less water[15]. From the magnetic susceptibility of water at 263° K. (Fig. 3) and of normal and tumour tissue (Fig. 2), an increase in the water content of the host tissue over the normal tissue of 5·8 and 8·5 per cent can be calculated for the liver and hepatoma respectively. This agrees with the fact that hepatomas generally have a higher content of water than normal liver[13–15]. It is therefore very probable that the increased diamagnetism of the liver and tumour tissue in the host is due to an increase in water content compared with the normal tissue.

An interesting feature of the results in Fig. 2 is the shape of the susceptibility curves for the tissue from the control and host animals. The change in state pattern of water does not appear in the normal tissue, and yet it is known that normal liver tissue contains about 70 per cent water. At least part of the water in the normal and tumour tissue does not go through the normal phase changes, that is, the molecules do not appear to be free to associate in the usual manner. As discussed by Gortner[17], many experiments have been performed which show that forces at the surface of lyophilic colloids tend to bind water with greater force than the usual forces of association which ultimately arrange water molecules in an ice crystal lattice. Bound water in gelatin has been shown to remain unfrozen down to temperatures as low as 170° K. (ref. 18), and probably will remain unfrozen to much lower temperatures. The perplexing problem in trying to explain the magnetic susceptibility of normal tissue by bound water is the amount present. It is difficult to see why essentially all the normal tissue water is bound, as would have to be the case to explain the results in Fig. 2. Most investigators have reported bound-water values of 25–30 per cent or less for colloidal materials[17], which are considerably

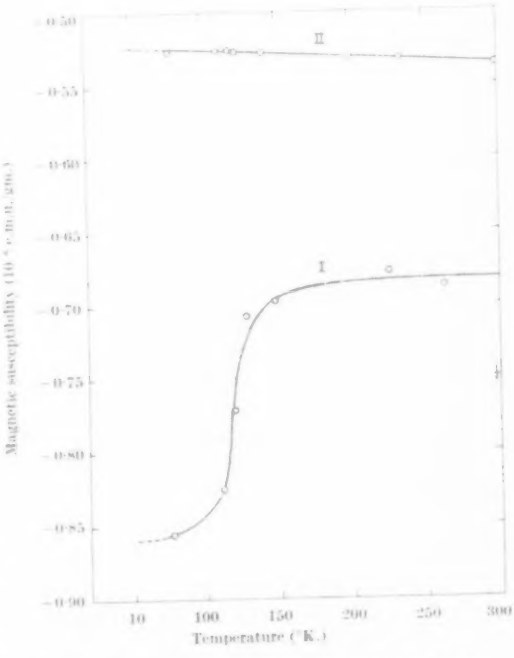

Fig. 4. Magnetic susceptibility of fresh egg white (I) and vacuum dehydrated egg white (II) as a function of temperature

less than is indicated by these measurements. Further work will have to be done to confirm the amount of bound water in normal tissue.

The decrease in the diamagnetism below 110° K. in the liver tissue and not in the tumour of the tumour-bearing host is not surprising. A small amount of paramagnetic or ferromagnetic impurity could easily account for the rise in the curve at the lower temperatures. It is known, for example, that both iron and cobalt are present in increased concentrations in the liver of tumour-bearing hosts.

In summary, it has been shown that the magnetic properties of transplanted hepatoma and normal liver tissue are different, and that the difference is probably due in a large part to the amount and form of the water held by the cells in the two types of tissue. The water in the normal cells appears to be bound, whereas that in the tumour tissue appears to be partially free water; however, this hypothesis will have to be confirmed by further experiment. If the pattern of magnetic susceptibility is found to be generally true for various kinds of tumour tissue, the measurement of magnetic susceptibility may be used as a diagnostic tool. With some refinements the method could be used on specimens as small as 1–2 mgm.

We wish to acknowledge the interest and help of various members of the National Cancer Institute. In particular, we wish to thank Drs. R. Kaiser, S. Ingbram, A. Hilberg and Mr. P. Lawrence for their stimulating discussions. Dr. H. P. Morris for supplying the test animals and transplanted hepatomas, and Mr. D. Trainor who helped to prepare the specimens. We are also grateful to Dr. H. Branson, of Harvard University, for his continued interest in this work.

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ACTIVATION OF FERRITIN SYNTHESIS AND INDUCTION OF CHANGES IN FINE STRUCTURE IN HELA CELLS *IN VITRO*: IMPLICATIONS FOR PROTEIN SYNTHESIS

By Prof. G. W. RICHTER

Department of Pathology, Cornell University Medical College, New York 21

WORK in my laboratory has provided evidence that the synthesis of the iron-containing protein, ferritin, can be activated in cells grown *in vitro* in tissue cultures. HeLa cells growing in a semi-synthetic medium produced ferritin within 4 hr. following addition of small quantities of ferrous sulphate to the medium. 5γ of iron per ml. of medium sufficed to bring about this result.

A strain of HeLa cells was obtained from Microbiological Associates, Inc., Bethesda, Maryland, and the cells were grown in an Earle–Eagle medium containing amino-acids, vitamins, minerals (excluding iron), streptomycin, penicillin, and horse serum (10 per cent by vol.). No iron was demonstrable in this medium by standard analytical tests sensitive to concentrations as low as 0·03 γ/ml.[1]. Control tests for iron, performed on acid digests of packed HeLa cells, grown during 2 weeks in 5 ml. of this medium, revealed minute amounts of iron, consistent with the presence of iron-containing enzymes.

Ferritin was demonstrated by means of electron microscopy on sectioned cells[2,3], and by chemical isolation using cadmium sulphate[4]. Furthermore, using established procedures[5,6], both ferritin and apoferritin were isolated from cell homogenates with an ultracentrifuge, and were later identified in the electron microscope[7] and by means of precipitin tests with specific antisera, obtained from rabbits after immunization with solutions of crystalline human ferritin. Trivalent iron in the cytoplasm—and occasionally in the nuclei—of cells treated with ferrous sulphate was shown to be present by means of the Prussian blue test.

Sub-cultures carried in individual flasks or bottles for approximately one week were used. Measured quantities of freshly prepared sterile solutions of ferrous sulphate were added to yield final concentrations of iron ranging from 2 to 15 γ/ml. Afterwards, cells were taken for examination after 2, 4, 24 hr., and at intervals up to 2 weeks. In cultures kept longer than 3 days the medium was changed periodically, and to some of these ferrous sulphate was added a second time. Cells from control cultures, to which no iron had been added, were examined concurrently.

Representative results obtained with HeLa cells are shown in Table 1. The findings indicate clearly that ferritin synthesis occurred within 4 hr. after addition of ferrous sulphate. As judged from electron micrographs and from yields of chemical

Table 1. Production of Ferritin (Apoferritin) by HeLa Cells

Ferrous sulphate γ/ml. medium	Interval	Tests for ferritin (apoferritin)			
		Cell extracts		Crystallization (cadmium sulphate)	Electron microscopy of cells (*c*)
		Precipitin tests	Electron microscopy (*d*)		
0	0 (*a*)	–	–	–	–
5	2 hr.	–	*A*	not done	–
5	4 hr.	+	*F* and *A*	" "	+
5	24 hr.	+	*F* and *A*	" "	+ +
5	48 hr.	+	*F* and *A*	" "	+ + +
5 (*b*)	5 days	+	*F* and *A*	+	+ + + +
5 (*c*)	14 days	+	*F* and *A*	+	+ + + +

Notes: (*a*) Control cultures, same age as others. No iron added. (*b*) Medium changed after 3 days without addition of iron. (*c*) Medium changed twice. Ferrous sulphate added each time. (*d*) *F*, ferritin present; *A*, apoferritin present. Apoferritin identified by means of negative staining (ref. 7). (*e*) Only ferritin can be identified with certainty by this method.

extractions, the quantities of ferritin accumulating in HeLa cells increased as time went on. But it was also found that some HeLa cells from cultures grown in the presence of ferrous sulphate contained little or no ferritin. It is not clear at present whether these were cells that had synthesized little or no ferritin; whether they had synthesized it and disgorged it; or whether only apoferritin—not clearly visible in electron micrographs of sectioned cells—was present.

The earliest accumulations of ferritin were located within discrete cytoplasmic bodies, up to 1μ in cross-section, and similar in appearance to the 'siderosomes' described previously by me[2]. However, these bodies varied considerably. Some resembled 'myelin figures', others had a complex system of tubules, and still others also contained a relatively homogeneous material of low density to electrons (apoferritin ?). Frequently, they were situated in a cell segment close to an indenture in the nucleus. Cytoplasmic bodies of a novel kind were noted in HeLa cells taken three or more days after addition of iron (Fig. 1). Characteristically, those bodies were delimited by membranes and contained material of high density to electrons. In profile this material appeared in the form of circinate structures, with hollow centres and with walls measuring up to 200 Å. in cross-section. Arrays of ferritin molecules often adjoined the dense walls. Cytoplasmic deposits of partly hydrated ferric oxide[8] were also noted. In samples taken from cultures 24 hr. after addition of ferrous sulphate a small proportion of cells contained intranuclear collections of ferritin molecules.

No ferritin or apoferritin was found in cells from control cultures to which no iron had been added.

Thus, the addition of ferrous sulphate to the HeLa cell cultures had two consequences: apoferritin synthesis, and the reaction of the apoferritin with iron, yielding ferritin.

Further results have indicated that apoferritin synthesis can be initiated in HeLa cells by very small concentrations of iron (< 1 γ/ml.), and that apoferritin is synthesized within 2 hr. after addition of iron—before ferritin iron micelles are detected in cells with the electron microscope. This is in agreement with evidence showing that in the liver apoferritin is synthesized first, and iron incorporated later into apoferritin[9].

It is not clear yet whether any of the aforementioned cytoplasmic organelles are sites of apoferritin synthesis, whether they are involved in the incorporation of iron into apoferritin, or whether they are concerned with the disposition of ferritin or apoferritin following synthesis elsewhere in the cell. Judging from present hypotheses on the mechanism of protein synthesis, the production of apoferritin might be initiated by intranuclear synthesis of specific RNA. The latter may then be moved into the cytoplasm[10].

One can infer that the HeLa cells possess an inherent capacity to synthesize ferritin; that this capacity has been retained after many years of cell division *in vitro*, and that therefore it is connected in some way with the cell genome. Further experiments are in progress to determine whether the primary effect of iron is intranuclear or intracytoplasmic, and to learn more about the mechanisms of the phenomena reported.

It is evident that the methods described here are applicable to controlled studies of protein synthesis in relation to the fine structure of cells, to their chemical constitution, and to their function. The methods are also relevant to investigations of immune mechanisms in which ferritin can be used as antigen.

Fig. 1. Part of cytoplasm of HeLa cell from culture kept 3 days in medium containing 5γ of iron per ml. Note organelle (*H*) at upper left, delimited by membrane and containing: (1) ferritin molecules represented by small particles, ~ 60 Å diam. (FeOOH micelles); (2) larger opaque bodies. A larger organelle (lower right) contains bodies (*C*) with opaque walls (~ 200 Å.), and non-opaque centres. Ferritin molecules are situated close to these bodies and within them. (× 100,000)

This work was supported by grants from the U.S. Public Health Service (*A* 1239 and *A* 823), and from the Rockefeller Foundation.

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RADIATION CARCINOGENESIS AT HIGH DOSE-RESPONSE LEVELS: A HYPOTHESIS

By Prof. ARNOLD E. REIF

Biochemistry Section, Department of Surgery, Tufts University School of Medicine, Boston City Hospital, Boston, Mass.

CARCINOGENESIS and cytotoxicity are two of the most important biological effects of ionizing radiation. The present hypothesis is an attempt to unify the concepts of their action[1]. It states that carcinogenesis and cytotoxicity act in opposition and together produce the overall relationship between radiation dose and tumour incidence that is found experimentally. The hypothesis has application to radiation therapy, and has been used to estimate the relative carcinogenic potencies of radium and strontium-90.

No assumptions are made regarding the detailed mechanism of radiation carcinogenesis, irrespective of whether in a given situation it is a primary process caused by a somatic mutation, or a secondary process caused by, for example, liberation of an oncogenic virus, or by creation of hormonal imbalance. Similarly, no assumptions are made regarding the normal defence mechanisms of the host against incipient cancer cells. Instead, consideration is confined to factual presence or absence of developing cancer cell clones. Complexities arising from the widely varying response to a carcinogenic stimulus depending on hormonal status[2] and functional integrity of the reticulo-endothelial system[3] will be discussed in a future publication.

The hypothesis assumes that the carcinogenic change is a rare but specific type of cell damage that occurs short of death of the cell. Since damage to cellular material increases as the dose of radiation is increased[4], so does carcinogenesis and the resultant incidence of tumours[5], until a maximum is reached. Beyond this maximum, the cell-killing effects of radiation would be expected to outweigh increasing carcinogenesis, resulting in a progressively lower incidence of tumours.

In fact, this expected behaviour occurs both with external radiations and with internal emitters. External cobalt-60 γ-rays given to mice in various constant daily doses resulted in a peak incidence of thymic lymphoma at 32 r./day, while at 56 r./day tumour incidence had dropped again to the level of unirradiated controls[6]. External X-rays given in a single dose to mice resulted in a peak in leukaemia incidence[7]. Injections of internal emitters such as radium, strontium-90 or calcium-45 into mice gave curves for bone tumour incidence showing sharp maxima[8]; injections of iodine-131 into rats gave similar incidence curves for thyroid tumours[8,9].

The lower portion of Fig. 1 illustrates the four main types of curves for tumour incidence found experimentally (curves *C*). While the abscissa expresses dose of a radioisotope deposited internally, curves *C* in part also represent tumour incidence induced by external radiations or by radiomimetic chemicals.

In the upper portion of Fig. 1, curve *C* has been split into two hypothetical curves *A* and *B*, which together produce *C*. Curve *A* represents 'pure' carcinogenesis, that is, carcinogenesis *in* the absence of other radiation effects that may counteract it. Curve *B* represents the combined cytotoxic effects of radiation on tumour cell clones, which prevent the development of all such clones in a percentage of the irradiated animals. At any dose-level, the percentage *C* of animals developing gross cancer during their life-span is the product of the percentage of animals with incipient tumour clones (*A*) and the fraction of animals in which all incipient tumour clones have not been eradicated (1–*B*/100), or:

$$C = A(1-B/100) \qquad (1)$$

Fig. 2 illustrates dissection of the cytotoxic process (curve *B* of Fig. 1) into two components, namely, eradication of tumour cells (curve *D*) and eradication of normal cells (curve *E*), which can cut short the life-span of the host before tumour clones have had time to develop into gross cancer. At any given dose-level:

$$1 - B/100 = (1 - D/100)\,(1 - E/100) \qquad (2)$$

The need for Fig. 2 can be eliminated by excluding animals which died from causes other than cancer during an experiment. With this correction, curve *B* in Fig. 1 is replaced by curve *D* and represents cytotoxicity against tumour.

Fig. 1 suggests explanations for the carcinogenic properties of a given external radiation, internal emitter or radiomimetic chemical[10]. Thus, production of osteogenic sarcoma in mice[8] places strontium-90 in or close to the highly carcinogenic grade 3, whereas radium falls into the medium carcinogenic grade 2. Apparently the short-range (35μ) and localized dose distribution[11] surrounding microscopic radium deposits in bone is better suited for killing any incipient cancer cells by continuing radiation than the longer range (6,000μ) and more diffuse dose distribution from strontium-90 and its daughter yttrium-09. Production of thyroid carcinomata in rats[9] classifies iodine-131 in the low carcinogenic grade 1, which differs from grade 2 in that cytotoxicity occurs at lower radiation doses than carcinogenicity. Grade 0 illustrates how a strong mutagen

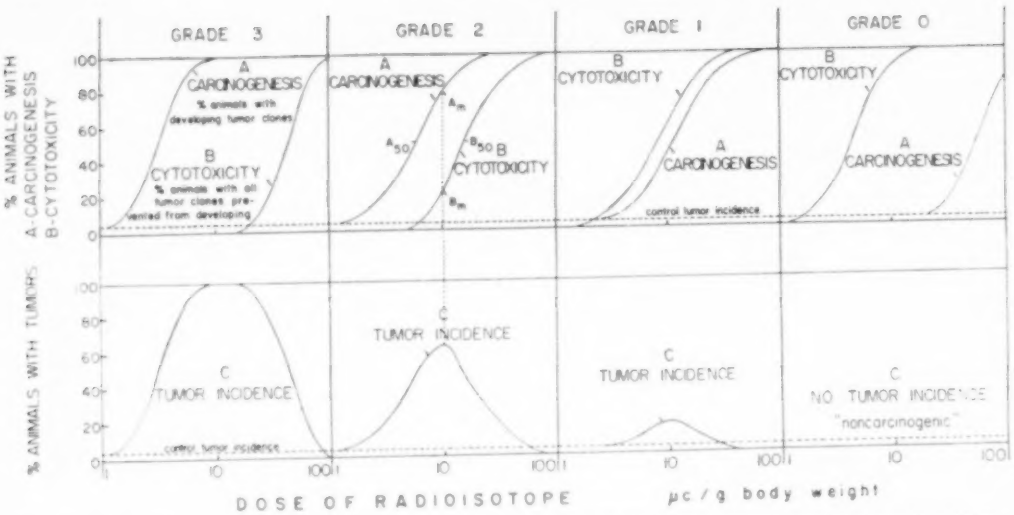

Fig. 1. Idealized curves *C*, of percentage of animals injected with a radioisotope that develop tumours, covering a range from highly carcinogenic (grade 3) to non-carcinogenic (grade 0). The overall shapes of the tumour incidence curves *C* are held to be the resultants of the opposing actions of carcinogenesis (curves *A*) and cytotoxicity (curves *B*)

such as acrolein may be non-carcinogenic[14]; cytotoxicity (in this case, acute lethality at a relatively low dose[13]) may predominate over carcinogenicity to such an extent that no gross tumours can occur. For any radiation, the carcinogenic potency evoked may depend on the mode of administration, the tissue irradiated, and the biological and genetic characteristics of the host.

Looking at Fig. 1 from the point of view of radiation therapy, the most carcinogenic dose-levels may lie just short of those giving complete cytotoxicity and therefore presenting no danger of carcinogenesis. This stresses the well-known importance of irradiating tumour masses with the highest dose-levels that can be tolerated by the patient. Irradiation of fringe areas or irradiation of normal tissues by therapeutic doses of radioisotopes should be minimized, since doses in the optimum carcinogenic range may be delivered. Because of the long latent period of radiation carcinogenesis in most body tissues, these latter considerations may apply only for younger patients.

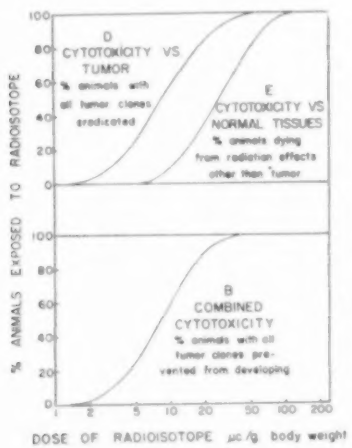
D
CYTOTOXICITY VS TUMOR
% animals with all tumor clones eradicated
E
CYTOTOXICITY VS NORMAL TISSUES
% animals dying from radiation effects other than tumor
B
COMBINED CYTOTOXICITY
% animals with all tumor clones prevented from developing
% ANIMALS EXPOSED TO RADIOISOTOPE
DOSE OF RADIOISOTOPE μc/g body weight

Fig. 2. Idealized curves, illustrating that overall cytotoxicity of an injected radioisotope against development of gross tumours (curve *B*) is held to be the resultant of cytotoxicity both against tumour (curve *D*) and against normal tissues (curve *E*)

Quantitative results are obtained by assuming that curves *A* and *B* are similar continuous *S*-shaped curves that are linear and of equal slope over their central portion. This assumption of equal slopes can be eliminated by use of equation (5) below. Curve *A* is identical with the upswing portion of curve *C* for grade 3 tumour incidence (Fig. 1), according to equation (1). While the curves for tumour incidence for strontium-90 and for calcium-45 barely miss[8,14] falling in grade 3, they do have an *S*-shaped upswing portion. For carcinogens other than ionizing radiation, grade 3 incidence curves are obtained with ultra-violet radiation[15] (which is also cytotoxic[16]) and with certain chemical carcinogens[17], and these curves are generally *S*-shaped. Similarly, curve *B* has been judged to be *S*-shaped.

At the optimum tumour dose, with tumour incidence maximal at C_m per cent, the corresponding ordinates A_m and B_m of curves *A* and *B* are related by:

$$B_m = 100 - A_m \qquad (3)$$

$$A_m = 10\sqrt{C_m} \qquad (4)$$

Curves *A* and *B* can be constructed graphically, provided the experimental curve *C* is known. Initially, curve *C* is drawn on semi-logarithmic paper. Next, the start of curve *A* and the end of curve *B* are traced on a second sheet, to correspond respectively with the start and with the inverted end of curve *C*. Curves *A* and *B* are continued to pass through respectively A_m and B_m, which are evaluated from equations (4) and (3). Finally, the curves are completed and if necessary replotted, such that equation (1) is satisfied by all points.

An additional refinement of questionable value is to eliminate the requirement for equal slopes of the linear portions of curves *A* and *B*. This necessitates replacement of equation (4) by the equation:

$$A_m = 10\sqrt{\left(\frac{a}{b}C_m\right)} \qquad (5)$$

where a and b are the respective slopes read from curves A and B constructed using equation (4), and A_m may lie only between C_m and 100 per cent. The new values of A_m and B_m can be used to re-plot curves A and B.

Points A_{50} and B_{50} are read off curves A and B (see grade 2 curves in Fig. 1) as the LD_{50} doses for carcinogenesis and cytotoxicity, respectively. The inverse dose ratio, B_{50}/A_{50}, is a measure of potency for carcinogenesis relative to cytotoxicity, that is, of the carcinogenic–cytotoxic potency. However, the value of this quantitative result is no greater than the validity of the assumptions on which it is based.

In applying this method to Finkel's results[8-11], integral curves of type C had to be constructed from differential curves of 'tumour-rate' in the case of radium and calcium-45. Using these comparable results resulting from a single injection in mice, the approximate values of the carcinogenic–cytotoxic potencies for radium, strontium-90 and calcium-45 were respectively 1·7, 7·0 and 6·1. When more suitable experimental data are available, better estimates will be possible.

Helpful criticism from Drs. Shields Warren, Robley D. Evans and Max Ritvo, and overall support by U.S. P.H.S. grant No. CY-4469, are gratefully acknowledged.

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EFFECTS OF GLUTAMINE AND ASPARAGINE SUPPLEMENTS IN THE DIETARY REGIMEN OF THREE PHENYLKETONURIC PATIENTS

By Dr. BARBARA H. BOWMAN* and Dr. F. J. KING†
Department of Zoology, University of Texas, Austin 12

PHENYLKETONURIA is an inherited condition which is characterized by a biochemical abnormality and usually by extreme mental retardation. The biochemical anomaly is the inability of the body to break down phenylalanine into the forms in which it can be used[1]. Instead, phenylalanine enters the blood stream in an unchanged form, most of it being converted later into phenylpyruvic acid and excreted in the urine[2].

Although many aspects of phenylketonuria are at present incompletely understood, much information has emerged from work carried on over a period of years. Through elimination of phenylalanine from the diets of phenylketonurics, abnormally high concentrations of the decomposition products of phenylalanine have been significantly lowered[3,4]. There is indirect evidence that this diminution of the decomposition products of phenylalanine is accompanied by improvement in mental function, especially in young subjects[5,6].

The toxicity of some of the metabolites of phenylalanine has been established, but there has been no evidence that phenylalanine *per se* is toxic[7,8]. The process by which phenylalanine is converted to phenylpyruvic acid in phenylketonuria is probably that of transamination. Meister, Udenfriend, and Bessman in 1956 gave evidence of the involvement of transamination in the formation of phenylpyruvic acid when they reported the reduction of this compound in phenylketonuric subjects to whom oral doses of glutamic acid, glutamine and asparagine were administered over a period of 12 hr.[9].

The aims of the present work were to decrease the phenylpyruvic acid phenylalanine ratio in phenylketonuric subjects through transamination by increasing the concentration of available amino donor and to study the effects of this in the phenylketonuric patients over a period of several months. Three phenylketonuric siblings were fed selected amino-acids under controlled conditions for approximately four months. A fourth affected child received a placebo. Daily urine specimens were collected from each subject for a few weeks before and during the entire period of administration of supplements. In the last weeks of the work one urine specimen was collected from each subject once a week. Urinary phenylpyruvate-levels were determined by a modification of the method of Penrose and Quastel[10]; urinary phenylalanine was determined by paper chromatography[11].

Subject I was a 21-year-old female who had an intelligence quotient (*I.Q.*) score of 18 before the amino-acid administration was begun. After the collection of daily urine specimens from her for a period of 5 weeks, she was given 3 daily doses of 7·3 gm. of L-asparagine over a period of 21 weeks, during

* Research Scientist of the Genetics Foundation of the Department of Zoology, University of Texas.
† Research Associate of the Department of Educational Psychology, University of Texas.

which time daily or weekly specimens were also collected. Mental performance was tested once before and twice during the period in which L-asparagine was being given, and an increase of 9 points in *I.Q.* score was observed at the end. Although a significant decrease of phenylpyruvic acid excretion in this subject was not apparent during the treatment, there was a definite decrease in the urinary phenylpyruvic acid–phenylalanine ratio. The *t* value for the significance of the difference between pre-treatment and during treatment means was 2·75, the probability being beyond the 5 per cent level of significance (Table 1).

Table 1. Ratio of Urinary Phenylpyruvic Acid to Phenylalanine

Subject	Mean before treatment	Mean during treatment	Difference between means	*t*-Ratio	Degrees of freedom	Probability
I	0·134	0·094	0·404	2·750	5*	> 0·05
II	0·151	0·113	0·179	1·409	23	< 0·05
III	0·102	0·060	0·425	4·618	24	> 0·01
IV	0·119	0·106	0·098	0·351	18	< 0·05

* Degrees of freedom reduced to adjust for lack of homogeneity of variance of the two samples.

Subject II was a 19-year-old phenylketonuric male who had an *I.Q.* score of 12 before the amino-acid administration was begun. Urine specimens were collected daily from him for a period of four weeks, after which time he was also given daily doses of 21 gm. of L-asparagine for a period of 21 weeks. During this time daily or weekly specimens were collected. There was no significant decrease in phenylpyruvic acid excretion in this subject during the treatment, nor was there any change in his mental performance or in the phenylpyruvic acid–phenylalanine ratio. Two possible reasons for the failure of the asparagine to reduce the phenylpyruvic acid–phenylalanine ratio in this subject have been postulated. First, the subject had an average urinary concentration of phenylpyruvic acid which was approximately twice that of any other subject used in this work. Secondly, the attendants were unable to give this subject L-asparagine as regularly as the supplements were given to the other subjects.

Subject III was a 17-year-old phenylketonuric female whose *I.Q.* score before treatment was 21. Daily urine specimens were collected from her 11 weeks before she began receiving 3 daily doses of 3·3 gm. of L-glutamine. She received glutamine for 17 weeks during which time daily or weekly urine specimens were collected. In this subject glutamine feeding was accompanied by a significant decrease in the phenylpyruvic acid–phenylalanine ratio and a significant decrease in phenylpyruvic acid excretion. The *t* value for the decrease in phenylpyruvic acid–phenylalanine ratio was 4·6, the probability being beyond the 1 per cent level of significance (Table 1). An increase of 8 points in *I.Q.* score was noted at the end of the experimental period.

The fourth subject served as a control. He was an 11-year-old phenylketonuric patient who had an *I.Q.* score of 15 before the administration of the placebo. Daily specimens were collected from him 4 weeks before he started receiving the placebo. There were no changes in the *I.Q.* score, the urinary phenylpyruvic acid excretion, or in the phenylpyruvic acid–phenylalanine ratio during the period of administration of the placebo.

The results of this work contribute evidence to the hypothesis that in phenylketonuria phenylalanine is converted to phenylpyruvic acid by means of a transamination process which may be reversed by increasing the available amino donor. The reduction of the phenylpyruvic acid–phenylalanine ratio was accompanied by a slight but significant improvement in each subject's ability. No increase in *I.Q.* score was seen in the two subjects who showed no reduction in the phenylpyruvic acid–phenylalanine ratio. The direct cause of the increase in *I.Q.* scores in the two phenylketonuric subjects is unknown, although the decrease of toxic products formed from phenylpyruvic acid and its derivatives may be one possible influence[12].

This work was supported by a grant awarded to Dr. C. P. Oliver and Dr. R. P. Wagner by the Welch Foundation, Houston, Texas, and by National Institutes of Health grant *C*–4022.

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PHAGOCYTIC ACTIVITY OF THE RECTICULO-ENDOTHELIAL SYSTEM

Effect of *B.C.G.*

IT has been reported previously that the active œstrogens are strong stimulants of the phagocytic activity of the reticulo-endothelial system[1–4]. These results were found with both natural and synthetic œstrogens. It would appear that the configuration of the molecule, which confers œstrogenic activity, is also essential for reticulo-endothelial stimulation.

The present investigation was designed to ascertain the effect of *B.C.G.* on the phagocytic activity of the reticulo-endothelial system, to find out whether any non-œstrogenic substances also stimulated the phagocytes and to compare the results with those of other substances reported from this laboratory.

Thirty male white mice (*T.O.* Swiss strain) of 20–25 gm. body-weight were used in these experiments. Twenty mice each received one intravenous injection of 0·05 ml. of an 8-day culture of *B.C.G.* on Dubos medium. At weekly intervals, the phagocytic activity was measured in five animals by the rate of

disappearance of a known amount of specially prepared carbon from the circulating blood[4], the procedure used being that described in previous communications[1] and the total body phagocytic activity or phagocytic index being denoted by the symbol K. In all cases, after the assessment of phagocytic activity, blood-counts were made and the animals were then killed and the weights of the liver and spleen determined.

Ten of the animals were used as controls and showed a phagocytic index or K-value of $16 \pm 3{\cdot}8$.

The results are shown in Table 1. It will be noted that at the end of one week there is a slight increase in phagocytic activity. This increase is more marked at the end of the second week and reaches a peak at the end of the third week, when the K-value is 78 ± 34. Thereafter the phagocytic index commences to fall and, at the end of the fourth week, the K-value is 39 ± 21. The stimulation of phagocytic activity is accompanied by a corresponding enlargement of the liver and spleen, which is most marked at the end of the third week, when the K-value is highest and is due to hypertrophy of hepatic and splenic tissue.

Table 1. Effect of *B.C.G.* on the Phagocytic Activity of the Reticulo-Endothelial System

Duration of treatment	Phagocytic Index (K-value)	Weight of liver (gm.)	Weight of spleen (gm.)
1 wk.	$22 \pm 3{\cdot}6$	$1{\cdot}12 \pm 0{\cdot}10$	$0{\cdot}09 \pm 0{\cdot}03$
2 wk.	41 ± 20	$1{\cdot}37 \pm 0{\cdot}26$	$0{\cdot}13 \pm 0{\cdot}03$
3 wk.	78 ± 34	$1{\cdot}67 \pm 0{\cdot}19$	$0{\cdot}23 \pm 0{\cdot}05$
4 wk.	39 ± 21	$1{\cdot}52 \pm 0{\cdot}14$	$0{\cdot}17 \pm 0{\cdot}06$
Controls	$16 \pm 3{\cdot}8$	$1{\cdot}20 \pm 0{\cdot}09$	$0{\cdot}06 \pm 0{\cdot}01$

The total red-cell counts indicated a slight reduction in the number of red cells, but the total white-cell counts remained normal throughout the four weeks of treatment.

The above results are in general agreement with those of Biozzi *et al.*[6,7] and show that the reticulo-endothelial phagocytes can be stimulated by non-œstrogenic substances. It has also been shown by Böhme and Bouvier[8] that killed *M. tuberculosis* strain *B.C.G.* and some of its constituents stimulate the reticulo-endothelial system and fail to induce changes in the percentage distribution of leucocytes in the peripheral circulation.

T. Nicol
P. McKelvie
C. G. Druce

Effect of Tri-*p*-anisylchloroethylene, Dienœstrol and Stilbœstrol Diphosphate

In the case of diethylstilbœstrol, it was shown that the minimum dose required to stimulate the reticulo-endothelial phagocytes is about one hundred times greater than the œstrogenic potential of the substance[2], and that when treatment with diethylstilbœstrol is stopped the phagocytic activity returns to normal level in about 8 days[3]. Other workers, Biozzi *et al.*[10] and Heller *et al.*[11], have confirmed our findings of reticulo-endothelial stimulation by œstrogens.

This communication deals with the effect of tri-*p*-anisylchloroethylene, dienœstrol and stilbœstrol diphosphate on the phagocytic activity of the reticulo-endothelial system and on the blood.

Fifty male white mice (*T.O.* Swiss strain) of 20–25 gm. body-weight were used in these investigations. Groups of five animals were used for testing the various compounds. In the case of tri-*p*-anisylchloroethylene, five animals received one daily-dose of 0·5 mgm. in 0·05 ml. arachis oil subcutaneously for 6 days; five received 1 mgm. in olive oil orally for 6 days and five received a similar dose orally for 12 days. The dienœstrol-treated animals each received one daily dose of 0·5 mgm. in 0·05 ml. arachis oil subcutaneously for 6 days; and those treated with stilbœstrol diphosphate each received one daily dose of 0·5 mgm. in 0·05 ml. water subcutaneously for 6 days. Two days after each course of treatment was completed, the phagocytic activity was measured by the rate of disappearance of a known amount of carbon from the circulating blood[4], the procedure used being that described in refs. 1 and 3, and the total body phagocytic activity or total phagocytic index being denoted by the symbol K.

The liver and spleen are known to be the principal reticulo-endothelial organs involved in removing particulate matter from the bloodstream, and, using the combined weights of liver and spleen, Benacerraf *et al.*[12] have applied a corrective factor to the total phagocytic index to give a measure of the phagocytic activity per unit of reticulo-endothelial tissue. This has been called the unit phagocytic index, and has been found to vary for a given dose of carbon according to the following equation:

$$\text{unit phagocytic index} = \frac{\text{total body-weight of animal}}{\text{combined weights of liver and spleen}} \sqrt[3]{K}$$

Generally, when the total phagocytic index K is raised, the unit phagocytic index rises also, indicating increased phagocytic activity per unit of reticulo-endothelial tissue.

All the animals used in the present experiments remained in good health during the course of treatment.

Twenty of the animals were used as controls. One group of ten each received 0·05 ml. arachis oil subcutaneously once daily for 6 days, the total phagocytic index K and the unit phagocytic index being measured on the eighth day by the carbon method referred to above.

In all the animals after the assessment of phagocytic activity blood counts were made, and the animals were then killed and the weights of the liver and spleen determined.

The results are shown in Table 2, in which, for comparison, the effect of diethylstilbœstrol on the phagocytic activity of the reticulo-endothelial system is also included. It can be seen that all the substances examined are active stimulants of both total and unit phagocytic activity, and that when treatment with tri-*p*-anisylchloroethylene and diethylstilbœstrol was continued for 12 days, the total and unit phagocytic indexes remained high in both cases. The results also show that phagocytic stimulation is accompanied by a corresponding enlargement of the liver in the case of dienœstrol, stilbœstrol diphosphate and diethylstilbœstrol, which is usual with most active œstrogens, but no hepatic enlargement was found in the animals treated with tri-*p*-anisylchloroethylene.

None of the four compounds produced any change in the blood picture, since in all the animals the total

Table 2. Effect of Tri-*p*-anisylchloroethylene, Dienestrol and Stilbestrol Diphosphate on the Phagocytic Activity of the Reticulo-Endothelial System

Compound used	Daily dose	Total phagocytic index (*K*-value)	Unit phagocytic index	Weight of liver (gm.)	Weight of spleen (gm.)
Tri-*p*-anisylchloroethylene	0·5 mgm. in arachis oil subcutaneously for 6 days	54 ± 25	51 ± 8	1·11 ± 0·10	0·13 ± 0·02
	1·0 mgm. in olive oil orally for 6 days	83 ± 31	67 ± 5	1·21 ± 0·13	0·05 ± 0·01
	1·0 mgm. in olive oil orally for 12 days	87 ± 27	66 ± 6	1·18 ± 0·09	0·10 ± 0·01
Dienestrol	0·5 mgm. in arachis oil subcutaneously for 6 days	40 ± 12	45 ± 5	1·47 ± 0·09	0·13 ± 0·01
Stilbestrol diphosphate	0·5 mgm. in water subcutaneously for 6 days	40 ± 4	48 ± 4	1·49 ± 0·19	0·13 ± 0·04
Diethylstilbestrol	0·5 mgm. in arachis oil subcutaneously for 6 days	65 ± 12	45 ± 6	1·79 ± 0·2	0·11 ± 0·02
	0·5 mgm. in arachis oil subcutaneously for 12 days	76 ± 14	65 ± 5	1·59 ± 0·15	0·11 ± 0·02
Untreated controls		15 ± 4	40 ± 4	1·28 ± 0·12	0·09 ± 0·02
Arachis oil controls		12 ± 3	38 ± 3	1·27 ± 0·13	0·14 ± 0·03

red-cell count and the total and differential white-cell counts remained within normal limits.

In the animals given tri-*p*-anisylchloroethylene orally, the high unit phagocytic index, without accompanying enlargement of the liver and spleen, indicates that this oestrogen has produced intense phagocytic activity. This difference in the action of tri-*p*-anisylchloroethylene may be due to the fact that, although it possesses high oestrogenicity and structurally resembles stilbestrol, it differs significantly from the other synthetic oestrogens at present in clinical use. It is actually a pro-oestrogen which is stored in body fat, released gradually, then converted by the liver into a potent oestrogen, the result closely resembling natural oestrogen secretion.

Unpublished work in this laboratory has shown that an active oestrogen such as diethylstilbestrol stimulates the reticulo-endothelial phagocytes and increases the amount of gamma globulin in the serum to about twice the normal level, and that this reticulo-endothelial stimulation protects animals against virulent infections. In the case of tri-*p*-anisylchloroethylene, the high total and unit phagocytic indexes found in the present research, together with the known absence of the usual oestrogenic side effects, suggest that tri-*p*-anisylchloroethylene may be the oestrogen of choice for clinical use in stimulating the reticulo-endothelial system and thus increasing the body defence against infection.

In this research we gratefully acknowledge financial assistance from the Medical Research Council.

T. Nicol
D. L. J. Bilbey
C. G. Druce

Department of Anatomy,
King's College,
London, W.C.2.

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DIFFERENT PERMEABILITY OF CUTICULAR SHEATH IN NORMAL AND GUARD KERATIN FIBRES

By R. Z. DE LA BURDE*
Collagen Project, Armour and Co., Chicago

THE property of hair is largely ascribed to the keratin, a protein stabilized by extensive disulphide bridges. In addition, resistant non-keratinous constituents are distributed throughout the fibre, contributing significantly to its overall stability. Those minor components, which at present are not positively identified, can be found in each of three major regions of the hair cuticle, cortex and medulla[1]. Some unequivocal differences in composition and behaviour are known to exist among similar, as well as different, keratin structures in a single species. Even a fibre grown out of a single follicle is heterogeneous in its transverse and axial directions[2–4].

Normal and guard rabbit hairs are known to differ in their pigmentation, diameter and extent of

* Present address: Deutsches Wollforschungs Institut, Rheinisch-Westfalische Technische Hochschule, Aachen, Germany.

modulation[5], but no information is available concerning their differences in composition and behaviour. The following work establishes the variations in coalescence and composition between normal and guard hairs of rabbit skins, classified organoleptically and physio-chemically to the second class. The differences in coalescence of cuticular membrane between fibres were characterized on the basis of their resistance to the penetration of aniline black and acridine orange.

In order to protect collagen from the damaging effect of components of the aniline oxidative bath, the samples were pretreated with chromium and fat solutions which introduced 11·2 per cent fat substances and 0·3 per cent chromic oxide. The ash content of the sample was 4·7 per cent and the moisture varied between 9·8 to 10·6 per cent. The hair cover was characterized by a 14·2 E.D.S. (elasticity, density, softness) value, 6·3 per cent abradability and its strength of setting in the corium was 13·2 kgm./cm.^{2} (ref. 6). The skins were exposed to acridine orange according to the method applied by Jarrett *et al.*[7]. Aniline black was applied to the hair by briefly brushing with a freshly prepared solution containing 7·5 per cent aniline hydrochloride, 2·8 per cent potassium chlorate and 2·8 per cent copper sulphate. The skins were dried for 24 hr. at approximately 45° C. with the initial relative humidity of 65 per cent and an air velocity of 0·5 m./sec. The skins were tumbled in sawdust and combed thoroughly in order to remove aniline oxidation products absorbed on the cuticle. The procedure was repeated 1–4 times. After each operation, 0·5 cm.^{2} samples were cut from the corium side and used for the cross-sectional examination of the hair cover. The entire amount of hair from each sample was wrapped into a compact bundle, with a thread wound in a tight spiral form. The tight bundle was immersed into acetone-celluloid glue, freed of its excess, dried and cross-sectioned with a Hardy microtome. In order to prevent distortion of the fibres, the specimens were covered with cedar oil and then examined in a drop of glycerine under the microscope. For each sample the ratio of normal to guard hair resisting the formation of nigro- and pernigro-aniline in the cortex was determined. The samples treated with acridine orange were examined in a similar manner by fluorescence microscopy for the presence of red fluorescence in the medulla of the fibres.

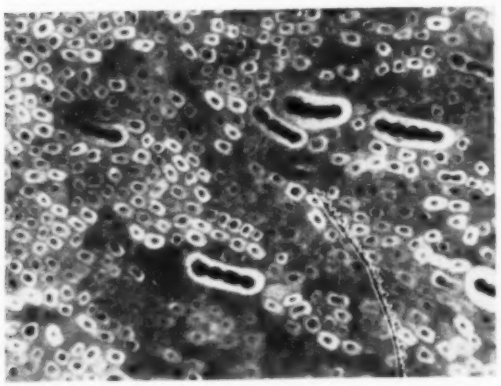

Fig. 1. Cross-section of rabbit hair bundle

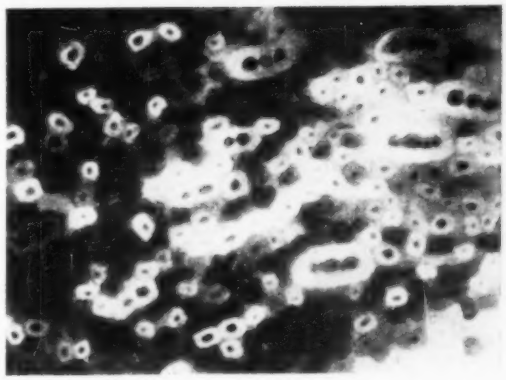

Fig. 2. Hair exposed twice to aniline black

Rabbit skins possess a great excess of normal hair (Fig. 1); its ratio to guard hair lies in the proximity of 1 : 37 bands of square and round shapes, which vary in width from $\frac{1}{8}$ to $\frac{1}{2}$ of the fibre diameter. Less than 10 per cent of total normal hair has no medulla. The guard hair is randomly distributed throughout the area of the skin. Its medullar bands vary from 2 to 8, depending on the cross-sectional region of the fibre. The ends of hair have no medulla. Microscopic examination of the dyed samples revealed that the guard hair is considerably more resistant to the penetration of acridine orange and aniline black than the normal hair (Fig. 2). The impermeable membrane in guard hair is the cuticular sheath. Wherever the cuticle was penetrated by the compound, it was found that the staining or the fluorescence was equally distributed throughout the cortex and medulla. Evidently the subcuticular resistant components which act as a cortical cell membrane[8,9] do not prevent an even distribution of the coloured compounds in this region. Neither acridine orange nor aniline black showed the differences in segmental keratinization of cortex in normal and guard hair[10].

Quantitative evaluation of the results summerized in Table 1 indicates that the cuticle of normal hair has a higher permeability to aniline than to acridine orange. The observed differences can be principally attributed to a smaller steric hindrance of the inter-chain bonds and non-keratinous substances towards the penetration of lower molecular weight aniline. The incorporation of fluorochrome into the medulla of normal hair is related to the number of exposures to the acridine orange. The cuticular membrane of guard hair is impermeable to this dye regardless of the number of treatments, whereas its resistance to the penetration of aniline decreases gradually.

Table 1. Differences in Permeability of the Cuticle in Normal and Guard Hair

No. of exposures to dye	Ratio of resistant normal to guard hair		Total percentage of dye-permeable fibres	
	Aniline black	Acridine orange	Aniline black	Acridine orange
0	31·8 : 1	31·8 : 1	0	0
1	15·4 : 1	19·2 : 1	52·2	38·4
2	10·2 : 1	10·9 : 1	80·6	55·6
3	7·7 : 1	4·3 : 1	87·4	78·2
4	4·8 : 1	1·2 : 1	95·7	90·8
5	4·2 : 1	0·2 : 1	99·3	95·2

The rate of changes in the permeability of cuticular sheaths in normal and guard hair exposed to the aniline dye suggests that the treatment modifies progressively the protein structure. After three exposures, the ratio of both fibres resisting the distribution of nigro- and pernigro-aniline remains at the same level. Evidently some component of the dye decreases the structural resistance of the cuticular layer in guard hair to such an extent that its permeability resembles that found in normal hair. In order to establish the nature of this modification, the effect of single components on the dye permeability of guard hair was studied. It was observed that the potassium chloride and the hydrochloric acid evolved during the reaction of aniline influenced the structural resistance of the cuticle. Each pre-treatment with potassium chlorate followed by an introduction of aniline black and acridine orange changed the resistance ratio of normal to guard hair to the values corresponding to the effect of multiple dyeing listed in Table. 1. The observed effect of potassium chlorate on the cuticle of guard hair can be explained by its potential disulphide cleaving action, whereby cystine is converted to cysteic acid. It is known, however, that the action of oxidizing agents like peroxy-acids, H_2O_2, Cl and ClO_2 causes solubilization before cleavage of the disulphide bridges in keratins[7-11]. In the experimental conditions used in this work, potassium chlorate and hydrochloric acid did not render the protein soluble to any detectable extent. It was observed, however, that the pre-treated fibres solubilized up to 12 per cent on extraction with 0·1 *N* ammonium hydroxide.

High-temperature amino-acid analysis[12] showed that the proline and cystine contents of normal rabbit hair are 5·6 and 12·4 per cent, and in guard hair the corresponding values are 6·8 and 14·1 per cent. The results obtained for cystine were confirmed by the colorimetric method of Zahn *et al.*[13].

The observations reported here indicate that distinct differences exist in the properties of cuticular sheath of normal and guard hair grown from the topographically identical part of the corium. These differences can be explained by the varying extent of keratinization, the principal factor being the degree of disulphide cross-linkage in the cuticle of both fibres. On the other hand, the nature of the action of potassium chlorate and hydrochloric acid does not exclude the possibility that the cleavage of intercha'n forces occurs at sites other than disulphide bridges and possibly in the structure associated with keratin in the cuticle. It has been observed, for example, that collagen, which is not stabilized by cystine cross-linkages, diminishes rapidly during treatment with potassium chlorate, its typical properties characterized by tensile strength, maximum elongation, hydrothermal stability, etc. Comparative data on this material will be reported elsewhere later.

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EFFECT OF ŒSTROGENS ON ATHEROSCLEROSIS

By Dr. M. R. MALINOW and Dr. J. A. MOGUILEVSKY

Institute of Physiology, Buenos Aires Medical School

Effect of Œstradiol on the Oxygen Consumption of Arteries in Chickens

THE oxygen uptake (Qo_2) of the uterus is enhanced in the rat by the injection of œstrogens[1] and a similar action is shared *in vitro* by endometrium, placenta, mammary gland and adenohypophysis of human origin[2]; the Qo_2 of other organs, though, may be depressed under similar experimental conditions[3-4]. Besides the well-known effects of œstrogens on genital tissues, these hormones can increase atherosclerosis of the great vessels in birds as well as inhibit and reverse coronary lesions in cholesterol-fed cockerels[5]. Since atherogenesis may be modified through a direct hormonal action on the vessels themselves[6], we decided to investigate the effects of œstrogens on the arterial oxygen uptake.

Male white Leghorn chickens raised on a standard laboratory mash and of an approximate weight of 800 gm. were killed; both innominate arterial trunks were rapidly excised and incubated separately at 37° C. on a balanced saline solution[6] also containing penicillin, streptomycin and 0·05 per cent ethanol. In another group of animals, one innominate trunk, chosen at random, was also incubated, but 2 µgm./ml. œstradiol-17β (Δ-1,3,5(10)-œstratriene, 3,17β-diol, melting point 197° C.) was added to the medium, the contralateral artery being taken as control. Oxygen uptake was determined, after incubation for 1 hr., with the usual manometric technique[7] and the results, expressed as $\mu l.O_2/hr./mgm.$ of dry tissue, were compared using the *t*-test and tables of Fisher and Yates[8].

Results in Table 1 indicate that Qo_2 is similar in both innominate arterial trunks, although, as shown in Table 2, the oxygen uptake of arteries is increased by œstradiol.

Table 1. Oxygen Uptake of Innominate Trunks in the Chicken

Artery	No. of birds	Oxygen uptake ($\mu l.$ O_2/hr./mgm. dry tissue) (mean ± *S.E.*)
Right innominate trunk	6	2·124 ± 0·472
Left innominate trunk	6	2·137 ± 0·463

$t = 0·019$; $P > 0·90$

Table 2. Effect of Œstradiol-17β on Oxygen Uptake of Innominate Trunks in Chickens

Innominate trunk	No. of birds	Oxygen uptake ($\mu l. O_2$/hr./mgm. dry tissue) (mean ± *S.E.*)
Control	12	1·584 ± 0·210
(Estradiol-17β (2 μgm./ml.)	12	3·714 ± 0·534

$t = 3·769$; $P < 0·01$

Despite the fact that the present findings in connexion with the problem of atherosclerosis are of questionable significance, they indicate clearly that œstradiol is able to modify arterial metabolism through a direct action on the vessels themselves. Although results obtained *in vitro* may not be related to conditions prevailing in the living organism, it seems appropriate to mention here that local effects of œstrogens on arteries have also been demonstrated as an enhanced activity of alkaline phosphatase in incubated aortas of chickens[9] as well as in connexion with certain aspects of lipid metabolism[10].

Effect of Incubated Arteries on Œstradiol-containing Media

It has already been demonstrated[5,11,12] that œstrogens prophylactically inhibit and therapeutically reverse coronary atherosclerosis in cholesterol-fed cockerels, even in the absence of any influence on aortic atherogenesis. Intimate mechanisms involved in these effects are not known, although recent findings seem to indicate that œstrogens may modify atherogenesis through a direct action on the arteries themselves[5]. Evidence bearing on such a direct action of œstrogens on arteries includes the demonstration of radioactive material within arterial walls after the injection of tritium-labelled œstradiol-6,7 [13], enhancement of alkaline phosphomonoesterase activity in aortæ incubated with œstradiol[9] and increased oxygen uptake of arteries brought about by adding œstradiol *in vitro*. Furthermore, the well-known actions of œstrogens on blood lipids as well as on the endocrine glands, although they cannot be totally discarded in this respect, have been found not to be correlated with the arterial modifications induced by the hormones[14].

In this work, a different approach has been used in order to study the possible relationships of œstrogens and atherogenesis, namely, the determination of the endocrine activity of nutrient media where different arteries from chickens were incubated with or without œstradiol.

Fifteen white Leghorn cockerels fed on commercial mash were used. The aorta, the coronary and the carotid arteries were aseptically removed; a low-power magnifier was used to dissect the coronaries, no effort being made to free them completely from adventitial fat. In groups of 3 chickens, the coronary arteries and aortic or carotid segments of an approximate similar weight were incubated during 72 hr. at 37 ± 1° C. in modified roller tubes as described[9], using approximately 2 ml. of balanced saline medium[6] also containing 30 per cent bovine serum, 0·05 per cent ethanol, penicillin and streptomycin. Incubation was also carried out with similar media containing 2 μgm./ml. of œstradiol-17β (Δ-1,3,5(10)-œstratriene, 3,17β-diol, melting point 197° C.); the media were changed every 24 hr., pooled and kept at −20° C. until used. All media were then similarly diluted in order to attain a theoretical concentration, for those containing the hormone, of 8·33 μgm./100 ml. of medium. They were then injected into groups of 10–12 immature female Swiss albino mice, 7–12 gm. weight, according to the method of Astwood[15] modified as follows: the animals received 2 subcutaneous daily injections of 0·2 ml. during 3 days (a total theoretical dose of 0·1 μgm.), and were killed with ether 18 hr. after the last injection; the mice were then weighed, the internal genitalia dissected under a low-power magnifier (ovaries, uterus, and the vagina as reached through the abdomen) and its weight indicated per 100 gm. of body-weight. Results were compared with Student's *t*-test and its significance evaluated using the tables of Fisher and Yates[8].

The method was standardized by injecting into groups of 10 immature female mice, nutrient media containing total doses of 0, 0·05, 0·1 or 0·2 μgm. œstradiol.

As can be seen in Table 3, the weight of internal genitalia of immature female mice increased proportionally to the injected dose of œstradiol. In Table 4, it is shown that the nutrient media without œstradiol showed no activity, whereas the amount of œstrogens in hormone-containing media incubated without arteries, with the aorta or with carotid arteries, was similar to the theoretical value. The activity of hormone-containing media incubated with coronary arteries, though, was lower than that expected.

Table 3. Weight of Internal Genitalia of Immature Female Mice injected with Œstradiol

Total dose (μgm.)	No. of animals	Internal genitalia (mgm./100 gm. body-weight) (mean ± *S.E.*)
0	7	165·3 ± 10·56
0·01	8	320·3 ± 12·24
0·05	9	492·6 ± 18·85
0·1	8	546·6 ± 24·74
0·2	7	636·9 ± 56·31

The present findings indicate, consequently, that coronary arteries from chickens, when incubated with œstradiol, are able to modify the activity of the hormone in the nutrient medium. Whether this change is secondary to adsorption of the œstrogen to the vessels or to molecular inactivation has not yet been determined. It is interesting that the aorta and the carotid arteries, when similarly incubated, are not able to induce such an inactivation. It is not possible to state at the present time whether this phenomenon is related to the known action of œstrogens which prevent coronary atherosclerosis in chickens without affecting the aorta and the great vessels in these animals[5,11,12]. Nevertheless, the experiments mentioned here, together with those already reported[9,13], indicate that œstrogens may interact with the arteries themselves, and that the action in atherosclerosis may probably be related to metabolic modifications brought about within the

Table 4. Weight of Internal Genitalia of Immature Female Mice injected with Nutrient Media from Incubated Arteries (Mean ± *S.E.*)

Description of media	No. of animals	Internal genitalia (mgm./100 gm. body-weight) Without œstradiol	No. of animals	Œstradiol 2 μgm./ml. (theoretical injected dose : 0·1 μgm./animal)
Without arteries	10	181·6 ± 7·10	10	526·8 ± 24·1†
Aorta	10	166·7 ± 16·7	10	656·8 ± 61·7
Carotid arteries	12	155·9 ± 6·20	13	506·8 ± 26·3
Coronary arteries	9	178·1 ± 24·1*	12	416·3 ± 27·0†

* From another set of experiments.
† $P < 0·01$ when compared, as indicated.

arterial walls. Further experiments are being completed and will be discussed in detail elsewhere.

Modification of Aortic Aerobic Metabolism in Rats by Gonadectomy

The importance of the sexual glands on the biology of normal arteries has not been studied thoroughly, although a few facts illustrate that such a relationship may exist. For example, the role of functioning gonads in human atherosclerosis is well known, men being more prone than women to coronary atherosclerosis, this difference tending to disappear after the menopause[16]. Furthermore, œstrogens are able to modify the development of atherosclerosis in several species[5], and a similar action is apparently shared by androgens in birds[17]. The following experiment demonstrates that the aerobic metabolism of the aorta is normally modified in rats through the influence of the gonadal glands.

Adult white albino male and female rats, weighing 150–250 gm., and reared on standard laboratory diet, were killed by brain concussion. The aorta was excised, freed from adventitial fat and the oxygen uptake determined during 1 hr. at 36·5° C. on pools of two arteries with the usual manometric technique[7] using a balanced saline solution[8] also containing streptomycin, penicillin and 0·05 per cent ethanol. Gonadectomy had been performed 30–40 days previously with a clean but not sterile technique under ether anæsthesia.

Table 5. Aortic Oxygen Uptake in the Rat

Groups	No. of determinations*	Oxygen uptake† (cl. hr.⁻¹/mgm. dry tissue)
Intact males	12	0·776 ± 0·055
Castrated males	6	2·546 ± 0·575
Intact females	10	0·680 ± 0·129
Spayed females	6	2·790 ± 0·294
1 vs. 2	11·283 $P < 0·001$	
1 vs. 3	0·690 $P = 0·50$	
3 vs. 4	6·677 $P < 0·001$	
2 vs. 4	0·418 $P < 0·70$	

* Each determination performed on pools of two animals.
† Mean ± S.E.

As can be seen in Table 5, the aortic oxygen uptake, which is similar in both sexes, is greatly accelerated by gonadectomy.

The mechanism through which the aerobic metabolism of the aorta is controlled has not yet been determined, although it is clear that the gonads share in this control. Current experiments performed in our laboratory indicate that it is probably mediated through a direct action of gonadal hormones on the arterial tissue. This work will be reported in detail elsewhere.

We wish to express our appreciation to Dr. B. A. Houssay and Dr. V. G. Foglia, who gave us helpful criticism.

This work was supported partly with grants from the Consejo Nacional de Investigaciones Cientificas y Técnicas de la República Argentina and the U.S. Public Health Service (H-3905).

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USE OF TRANSPARENT ADHESIVE TAPE IN THE PREPARATION OF MICROSECTIONS

By D. S. GOWERS and R. E. MILLER
Research Department, Rohm and Haas, Co., Bristol, Pa.

IN 1954, Palmgren[1] described the use of cellulose adhesive tape as a means of holding together large sections of hard or brittle specimens during the cutting operation. The technique for transferring the section from the tape to a slide was rather elaborate, and in 1959 W. E. Beckel[2] proposed a much simpler method using different adhesive tapes. Scotch tape No. 810 (Minnesota Mining Co.), was used for sections to be fastened to the slide with albumen, while 'Mystik Kylon' tape No. 6400 (Mystik Tape Products Div., Englewood Co., Inc.), was used with 'Celloidin' as an adhesive. The Scotch tape No. 810 was removed in 30 min. or less by treatment with organic solvents such as furan, chloroform and xylene, and we had no difficulty in using the same technique with tape samples supplied by Dr. W. E. Beckel. No sample we were able to buy, however, had a soluble adhesive, and we were informed by the Minnesota Mining Co.[3] that only certain Canadian batches of this tape have soluble adhesive; usually the adhesive is cross-linked and will not dissolve cleanly in any solvents. We purchased a wide variety of makes and types of adhesive tapes, and the only ones we found with soluble adhesives were 'Tuck' tapes Nos. 200 and 205, made by the Technical Tape Corp., New York 43. Only No. 200 had satisfactory tackiness. Beckel's method for Scotch tape No. 810 may be used with 'Tuck' tape, but it takes 1–10 hr. to remove the tape and adhesive with xylene, because the cellulose backing is not very permeable to the solvent; the larger the piece of tape the longer it takes.

Previous applications of the tape method have been to whole animals, or heavily sclerotized whole insects. We have applied the method as it stands to the sectioning of textile fibres. Our real modification, however, is to mount the sections without removing them from the tape. In this way, and with a suitable embedding technique, we have been able to section textile fibres and delicate aggregates of polymer particles which are soluble in molten paraffin wax, and in the organic reagents normally used in section preparation. The unaltered method used on paraffin-embedded textile fibres gives very high quality sections down to 1 μ, with rare failures.

The following is a typical example of the application of our modified technique to the sectioning of a solvent-sensitive specimen. 'Mystik Kylon' tape No. 6400 is used because of the thinness and flexibility of the backing.

Immerse the sample in polyvinylpyrrolidone solution (see 1 below) in an open dish. Put the dish in the vacuum oven at a temperature of 30–50° C. (depending on what the specimen will stand), and slowly pump down to about 28 in. mercury. Keep the oven in this condition for 2 min., and then bring it up to atmospheric pressure. Lift the sample from the solution with a spoon, taking up about 0·5 c.c. of solution, and pour the whole on to the flat surface of solidified embedding wax (see 2 below) in a Petri dish. The sample should be manipulated into the centre of a strip of the solution about 2 cm. long, and 3–5 mm. wide. Put the Petri dish in a desiccator over 50 per cent w/w sulphuric acid (about 35 per cent relative humidity), and let it stand there for three days. In this time the polyvinylpyrrolidone solution will dry down to a solid with the correct consistency for cutting. With a scalpel make two cuts in the wax, one on each side of the strip, so that the strip lifts away with a wedge of wax attached to it. After suitably trimming the length of the strip, embed it in a block of wax (see 2), and trim the block to a truncated pyramid so that the sample lies just below the upper surface.

Mount the block in the microtome, and cool it to 10–15° C. by blowing a jet of cooled air or nitrogen on it. After cutting down to the desired level, gently press a piece of 'Mystik Kylon' tape No. 6400 on to the exposed face of the specimen and cut the section rather slowly. The piece of tape will have a rectangle of wax on it, in the middle of which is a clear patch of polyvinylpyrrolidone containing the section. Trim the tape around the edges of the wax—it may now be handled with forceps and will not stick to everything that it touches.

Lay the tape on a slide with the wax side up. Put a drop of Farrants' medium (see 3 below) over the section, and drop the cover-slip into place. Stand a 10-gm. weight on the cover-slip, and put the slide into the vacuum oven at the temperature used for the impregnation with polyvinylpyrrolidone. Pump down until air bubbles begin to come out from under the cover-slip. Allow bubbling to go on for 2–3 sec., and then bring the oven rapidly to atmospheric pressure. Excess mountant is removed from the edges of the cover-slip with a wet brush, while the slide is rotated on a turntable. Bell's cement, or 'Murrayite' cement is excellent for sealing the preparation.

When fibres are to be sectioned they are treated as above, except that the polyvinylpyrrolidone embedded bundle is hung up on a wire rack and allowed to dry at 35 per cent relative humidity.

It is often possible to stain sections on the tape before mounting. Thus sections of acid ion-exchange beads may be stained with a variety of aqueous basic dyes, and basic beads may be stained with acid dyes, with little or no colour take-up by the tape. The feasibility of using any particular staining method can only be determined by trial.

If processing in aqueous solutions is not essential the equilibration time for the first embedding can be cut to one day in the open air, at any relative humidity, by impregnating with an alcoholic solution of Dow's 'Devlex *A* 515' resin (see 4 below), instead of polyvinylpyrrolidone. The oven temperature should not exceed 30° C. in this case, and a vacuum of only about 20 in. mercury is needed. The rest of the technique is as described above, except that the section is mounted in Hoyer's gum mastic medium (see 5 below).

The compositions used are as follows (all percentages are by weight):

(1) *Medium for the first embedding.* 43·5 per cent polyvinylpyrrolidone, Grade *K*-30 (av. mol. wt. 40,000); 13 per cent diethylene glycol as plasticizer; 43·5 per cent water. Glycerol may be substituted for diethylene glycol, but the film is more sensitive to relative humidity, and has only half the extension at break[4]. The above composition is suitable for sectioning without tape if the room humidity is between 30 and 40 per cent. For other humidities the amount of diethylene glycol may be changed, less being used for higher humidities.

(2) *Wax for the second embedding.* 48 per cent paraffin wax m.p. 58–60° C.; 50 per cent stearic acid; 1 per cent beeswax; 1 per cent carnauba wax.

This composition was found, by a factorial experiment at three levels for each component, to be suitable for direct sectioning of moderately hard materials. It has given excellent results in the above techniques. It was developed from a paraffin–stearic acid mixture, suggested by Preston[5], to give more coherent films on cutting.

(3) *Farrants' medium*[6]. 40 per cent water : 40 per cent gum arabic; 20 per cent glycerol.

(4) *Alternative first embedding medium.* 43 per cent 'Devlex *A* 515' (a copolymer of N-vinyl-5-methyl-2-oxazolidinone and vinyl acetate, made by the Dow Chemical Co.); about 14 per cent propylene glycol as plasticizer; 43 per cent absolute ethanol. For sectioning without tape this mixture gives a film which is very insensitive to room humidity. The following plasticizers may also be used: 8 per cent 1,3-butylene glycol, 8 per cent trimethylol ethane, or 8 per cent 1,2,6-tri-hydroxy-hexane, with 46 per cent 'Devlex *A* 515' and 46 per cent ethanol.

(5) *Hoyer's gum mastic mountant*[7]. Gum mastic dissolved in excess 95 per cent ethanol, filtered, and evaporated to the required consistency.

We wish to express our thanks to Dr. John O. VanHook, who suggested and supplied the plasticizers for the 'Devlex *A* 515' resin.

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LETTERS TO THE EDITORS

GEOPHYSICS

A Twilight Method of determining the Vertical Distribution of Ozone

Determination of vertical distributions of ozone from lunar eclipse observations[1] suggests the practicability of similar ground-based optical methods, provided 'screens' more amenable to experimental control than the Moon can be used. Alternatives are noctilucent clouds, atmospheric layers, balloons, and artificial Earth satellites. Noctilucent clouds are rather rare and beyond experimental control; ionospheric layers give very limited information[2], as do other atmospheric layers such as sodium[3]. Following a suggestion by Dr. V. D. Hopper of this Department, a method analogous to the lunar eclipse method has therefore been developed in Melbourne, for initial application to ground-based filter photometric observations of balloons at twilight.

Rays from the twilight Sun pass tangentially through the ozone layer to a balloon floating above a substantial part of the atmospheric ozone. This gives a very long path-length through the atmosphere, having an effective thickness of ozone which depends critically on solar zenith angle. The effective thickness (reduced to S.T.P.) reaches about 7–10 cm. for the optimum minimum height of the rays, depending on the amount of ozone and its vertical distribution. This gives rise to absorption due to ozone, near the maximum of the Chappuis band, of 30–50 per cent.

A ground-based observer can then measure the intensity of various wave-lengths scattered to ground from the balloon. This has an advantage over lunar eclipse observations, apart from the frequency and control of occurrence, in that direct measurements can be made in the laboratory of the scattering properties of the scattering surface in the absence of an intervening atmosphere.

As the balloon is not above the whole of the atmosphere, it is necessary to modify substantially the lunar eclipse theory. Denoting the total effective thickness of ozone traversed by $X = x_a + x_b$, where x_a is the effective thickness in the path from the Sun to the balloon, and x_b that between the balloon and the ground, then it can be shown that, for two different zenith angles, with effective thicknesses of ozone of X and X', we have:

$$X' - X = (\alpha_2\lambda_1^{-4} - \alpha_1\lambda_2^{-4})^{-1}\left[\lambda_1^{-4}\log\left(\frac{I_2}{I_2'}\cdot\frac{S_2'}{S_2}\right) - \lambda_2^{-4}\log\left(\frac{I_1}{I_1'}\cdot\frac{S_1'}{S_1}\right)\right] \quad (1)$$

for wave-lengths λ_1 and λ_2 having decadic extinction coefficients α_1 and α_2, respectively, where S_i denotes the scattering factor of the balloon (assumed to be a function of wave-length and angle of scattering), and I_i is the intensity at the ground, of wave-length λ_i.

The effects of Rayleigh scattering and non-selective scattering have been eliminated, as well as the effect of differing sensitivities to wave-lengths λ_1 and λ_2. It is assumed that the incident intensities, at the top of the atmosphere, of wave-lengths λ_1 and λ_2, do not change during the course of the observations, without requiring any knowledge of their value or ratio. The elimination of non-selective scattering is based on the assumption that such scattering only occurs in the path from balloon to ground, and that it is constant. This could be invalidated by drifting dust or smoke clouds, or by observations during which the tangential rays pass through layers of non-selective absorbers, as would occur when the depression of the Sun brought the minimum height too low in the atmosphere. In general, this last consideration may well restrict the method to the determination of the vertical distribution above the troposphere.

The right-hand side of equation (1) can be determined by measurement, while the left-hand side can be obtained in terms of the vertical distribution of ozone.

Consider the atmosphere divided into layers of thickness Δh_i km., each having a reduced thickness of ozone per km. of a_i. Then, neglecting the curvature of the Earth for the path from the balloon to the observer, which is reasonable for zenith angles of the balloon of less than about 60°, we have:

$$x_b = \sec Z_b \sum_{h_i=0}^{h_b} a_i . \Delta h_i \quad (2)$$

where Z_b is the zenith angle from the observer, of the balloon at a height h_b.

Between the Sun and the balloon the curvature of the Earth must be considered. Thus:

$$x_a = \sum_{h_i=h_{\min.}}^{\infty} a_i . \Delta l_i + \sum_{h_i=h_{\min.}}^{h_b} a_i . \Delta l_i \quad (3)$$

where

$$\Delta l_i = [(R + h_2)^2 - (R+h_{\min.})^2]^{1/2} - [(R+h_1)^2 - (R + h_{\min.})^2]^{1/2} \quad (4)$$

R is the radius of the Earth, $h_{\min.}$ is the minimum height of the tangential ray, and h_1 and h_2 are the lower and upper boundaries of the layers considered.

X may therefore be evaluated, for a given set of atmospheric layers, in terms of a linear sum of multiples of the unknown concentrations a_i, where $R + h_{\min.} = (R + h_0)\sin Z_0$ for the Sun at a zenith angle Z_0.

For known pairs of values of h_0, Z_0, and Z_b, it is thus possible to obtain a linear equation containing the unknown concentrations in each layer considered. Hence $(n + 1)$ sets of measurements, each corresponding to a particular position of the Sun and balloon, will give n independent equations of this type, which may then be solved for the unknown concentrations in n layers to give an approximation to the vertical distribution of ozone.

Large meteorological balloons in level flight[4] at 30–40 km. altitude are to be used for the initial observations. Narrow pass-band interference filters centred on 6150 Å. and 4400 Å. have been chosen for the photometer. The choice of 6150 Å. for the wave-length absorbed by ozone is governed by the interfering bands in the visible spectrum[5,6]. Interference is considerably less than in the case discussed by Dufay[5] due to the relatively short path through the troposphere.

The main practical difficulty in this method, using ground-based observation equipment, is that of eliminating the twilight sky background, which

changes in a very rapid and complex manner as the Sun sinks below the horizon. This requires that the field of view of the photometer be severely restricted by a diaphragm in the focal plane of an objective mirror or lens. Accurate tracking is necessary to keep a balloon within such a field of view. The accuracy to which the height of the balloon is determined will greatly affect the accuracy of the results. If the balloon is above the bulk of the ozone layer, the uncertainty in height can be regarded as equivalent to a corresponding margin of error in time (or solar zenith angle), since it leads to an uncertainty in the minimum height of the tangential ray.

The minimum height of the tangential ray reaches the troposphere for solar depressions of about 5° or 6°, depending on the height of the balloon. This allows only about 20–25 min. during which to take all the measurements, while the rate of change of atmospheric path makes it necessary to take the readings for a given path within about 10 sec. if an accurate distribution is to be derived.

The method outlined above has a number of limitations. It is restricted to clear sky observations. It determines the vertical distribution smoothed out over large horizontal distances, rather than the distribution above a particular geographical location. It will be largely restricted to stratospheric ozone, and to observations only twice a day (except perhaps in polar regions). Finally, it requires considerable skill and experience.

On the other hand, its great sensitivity to ozone in the upper layers of the atmosphere should enable solar and seasonal variations in the equilibrium region of the ozone layer to be studied with increased accuracy. The method may also be applied to other constituents of the upper atmosphere with comparatively little modification.

I am indebted to Drs. V. D. Hopper and J. E. Laby, and to Mr. K. B. Mather, for their advice and discussions, and to the Dunlop Rubber Co. for financial support.

A. B. Pittock

Physics Department,
University of Melbourne,
Parkville, N.2,
Victoria.

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Motion of Geomagnetic Field Lines

In a communication with the above title[1], I stated that trapped-particle orbits in the radiation belts follow the motion of the geomagnetic field lines. As this is incorrect, the conclusions reached in that communication cannot be applied to the behaviour of the radiation belts, and my criticism of a hypothesis put forward by Rees and Reid[2] was unfounded. A more satisfactory discussion of this hypothesis has been published by Malville[3].

C. J. Loughnan

Dominion Physical Laboratory Auroral Station,
Omakau, New Zealand.

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PHYSICS

Mercury-206: a New Natural Radionuclide

According to Cameron's mass formula[1], the value of Q_α for lead-210 (radium D) should be 3·566 MeV., which would indicate an alpha half-life of the order of 10^{19} years and an alpha-branching of the order of 10^{-9}. The same source gives 1·361 MeV. for the Q_β of the hitherto unknown mercury-206, which is formed from lead-210 by alpha decay. From a closed cycle of reactions, the sum of Q_α for lead-210 and Q_β of mercury-206 is found to be 5·0 MeV.; the absence of known alpha-branching in lead-210 further suggests that the Q_α for lead-210 does not appreciably exceed the value mentioned above. (This has been pointed out also by Prof. I. Perlman; private communication by Dr. K. Hyde.)

The ground-state of thallium-206 is reported to be 0^- (refs. 2 and 3), which would indicate a beta half-life of the order of one day for mercury-206 at the energy mentioned above. However, the beta decay of 4·2-min. thallium-206 (Q_β = 1·51 MeV.) exhibits a log (comparative half-life) value of 5·1, which is typical for an allowed transition; if it is assumed that this is the case for mercury-206 also, a half-life of about 10 min. is obtained. On the other hand, mercury-206 contains 126 neutrons which should increase its stability, and several attempts[4] have been made to detect it under the assumption that its half-life is relatively long.

We have detected the alpha-branching of lead-210 by rapidly separating the lead fraction from a radium D,E,F mixture. Preparations from 20–200 microcuries of lead-210 were used and the measurement was carried out in a gridded ion-chamber of the type described by Karras[5]. The measurements were begun about 7 min. after the beginning of the chemical separation and continued for about 1 hr.; during this time the polonium activity grew from less than one c.p.m. to hundreds of counts per minute. The alpha-branching of bismuth-210 was investigated in an analogous way, with results in agreement with those of Fink and Warren[6a,b]; results on both nuclides are given in Table 1.

Table 1

Nuclide	Half-life	Measured E_α (MeV.)	Branching
Lead-210	22 years	3·76 ± 0·06	(1·8 ± 0·5) × 10^{-6}
Bismuth-210	5 days	4·80 ± 0·05	(1·9 ± 0·4) × 10^{-6}

In order to investigate the properties of mercury-206, bismuth and polonium were first removed from a solution containing 4 millicuries of lead-210. The solution was then made 1 *N* with nitric acid, whereupon bismuth and thallium holdback carriers and about 40 μgm. of mercury carrier were added. After standing for 60–75 min. the mercury fraction was extracted with an equivalent amount of 0·005 per cent solution of dithizone in chloroform. The extract was scrubbed twice with 1 *N* nitric acid and evaporated on to a small aluminium cup which was counted with an end-window Geiger–Müller counter shielded with 20 cm. of iron.

The time needed for the separation proper was 2·5 min.; after this period, the thallium-206 daughter was retained and grew during the evaporation and mounting, which took another 2·5 min. A beta-decay graph obtained as an average of five measurements is shown in Fig. 1 (crosses) together with a decay curve calculated using 7·5 min. and 4·2 min. for the half-lives of mercury-206 and thallium-206, and

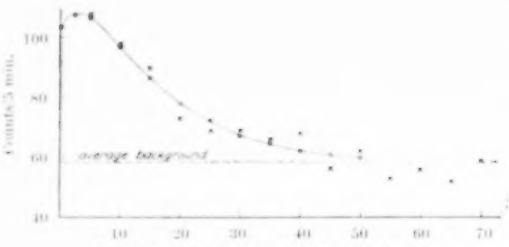

Fig. 1. Observed beta-decay of the composite mercury-206 thallium-206 activity (crosses; average of five measurements) compared with a decay graph calculated using 4·2 min. and 7·5 min. for the half-lives of thallium-206 and mercury-206, and assuming equal efficiencies of detection

assuming equal detection efficiencies for both activities. A value of (7·5 ± 1) min. is thus obtained for the half-life of mercury-206, while the closed cycle leads to a value of (1·2 ± 0·1) MeV. for Q_β.

We are indebted to Dr. Richard W. Fink, Dr. Goran Andersson, and Dr. Earl K. Hyde for many valuable suggestions, and to Prof. L. Simons for permission to use the equipment of the Van de Graaff Laboratory in some of the alpha-spectrometry measurements.

The investigation has been supported by the Finnish Atomic Energy Commission, the State Committee on Natural Sciences, the Chancellor of the University of Helsinki and Honkanen's Foundation.

A more detailed report of this work will be published by P. Kauranen in *Ann. Acad. Scient. Fenn.*

Note added in proof. Walen and Bastin-Scoffier (*J. Phys. Radium*, **20**, 589; 1959) measured for bismuth-210 E_α = 4·686 and 4·649 MeV.; our result is clearly too high.

M. Nurmia
P. Kauranen
M. Karras
A. Siivola
A. Isola
G. Graeffe
A. Lyyjynen

Institute of Physics,
University of Helsinki,
Finland.

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A Theory of Cold-Cathode Arc Movement in a Magnetic Field

When a cold-cathode arc is initiated in the presence of a transverse magnetic field, movement of the cathode root occurs in a direction mutually perpendicular to the arc current axis and the magnetic field lines. At atmospheric pressure the arc moves in the amperian direction; but at low pressure, motion in the reverse sense can occur. Experimental investigations have shown that in both these modes of motion the conditions in the cathode fall region are of primary importance[1,2], and thus an understanding of the processes occurring in this region is necessary to an explanation of arc motion. A mechanism for retrograde motion at low pressure has been described by Ecker[2]; but to date no satisfactory explanation of the normal amperian motion has been put forward.

The cathode fall may conveniently be divided into three zones[2]: (1) a space-charge zone very close to the cathode surface; (2) a transition zone, where the field is less than in the space-charge zone; (3) the contraction zone, where quasi-neutrality exists. It seems probable that for the cold-cathode arc, in which current densities of the order of 10^8 amp./cm.^{2} are generally believed to exist, a field-type of emission process is operative. If either the thermal[3] or individual[3-5] field emission mechanisms are postulated, a background field $\sim 10^7$ V./cm. is likely to be necessary in the space-charge zone. As the voltage across the fall region is always about 10 V. the extent of the space-charge zone must be less than λ^+, the ion mean free-fall distance, even at atmospheric pressure, though the field in this region will decrease somewhat away from the cathode surface. The small depth of the space-charge zone can be explained by assuming a progressive back-diffusion of electrons against the electric field[3].

For convenience, calculations of electron behaviour in the fall region may be made for two different cases with the limits:

$$(a)\ R > \lambda^- \qquad (b)\ R < \lambda^-$$

where R is the radius of an emitting area on the cathode. It can be shown that case (*a*) corresponds to the high-(atmospheric) pressure arc, while (*b*) is valid for the low-pressure arc. Only (*a*) will be discussed here since it is proposed to describe a model for amperian motion. As $R > \lambda^-$, and the extension of the space-charge zone, $d_s < \lambda^-$, a one-dimensional electric field results and electron movement in the space-charge zone will be essentially normal to the cathode surface. This is true despite the presence of the transverse magnetic field since the electric field is so large. In passing through the zone an electron will gain about 6–8 eV. energy. Current densities of about 10^8 amp./cm.^{2} have been observed for vacuum arcs as well as those operated at a pressure of several atmospheres, so that it would appear that the background field of about 10^7 V./cm. is affected little by pressure. Since also the cathode voltage remains sensibly constant at about 10 V. for a wide pressure-range, it would seem that both the energy gain in the space charge region and the depth of this region vary very little.

In the transition zone, the electrons will suffer many elastic collisions before they gain the few extra eV. required for an inelastic collision. It is almost certain that in air, which is considered here, ionization occurs by a series of electron impacts which raise the gas particle to successively higher excited levels[7], although thermal energy in this region will to some extent aid this process. In this zone the electrons, prior to excitation collisions, have a high random velocity, by virtue of their energy, but their drift velocity normal to the cathode surface is low, because of the many collisions which occur. The transverse magnetic field is thus able to deflect the electrons in the amperian direction.

By making a few simple assumptions, it can be shown that the extension of the transition zone, d_t, is given by:

$$d_t = \frac{\lambda^-}{2f^{1/2}} \cdot \tanh^{-1} \frac{2f^{1/2}}{E\lambda^-}(V_t - V_s) \qquad (1)$$

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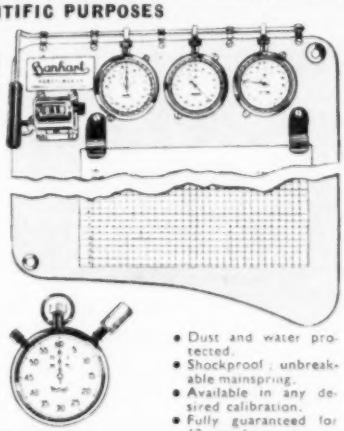

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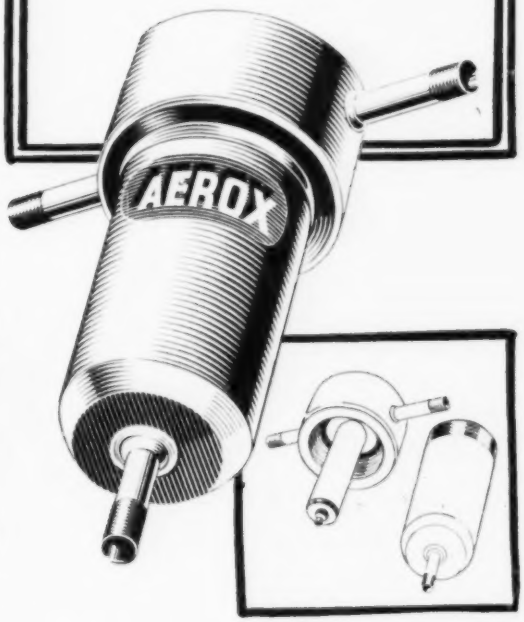

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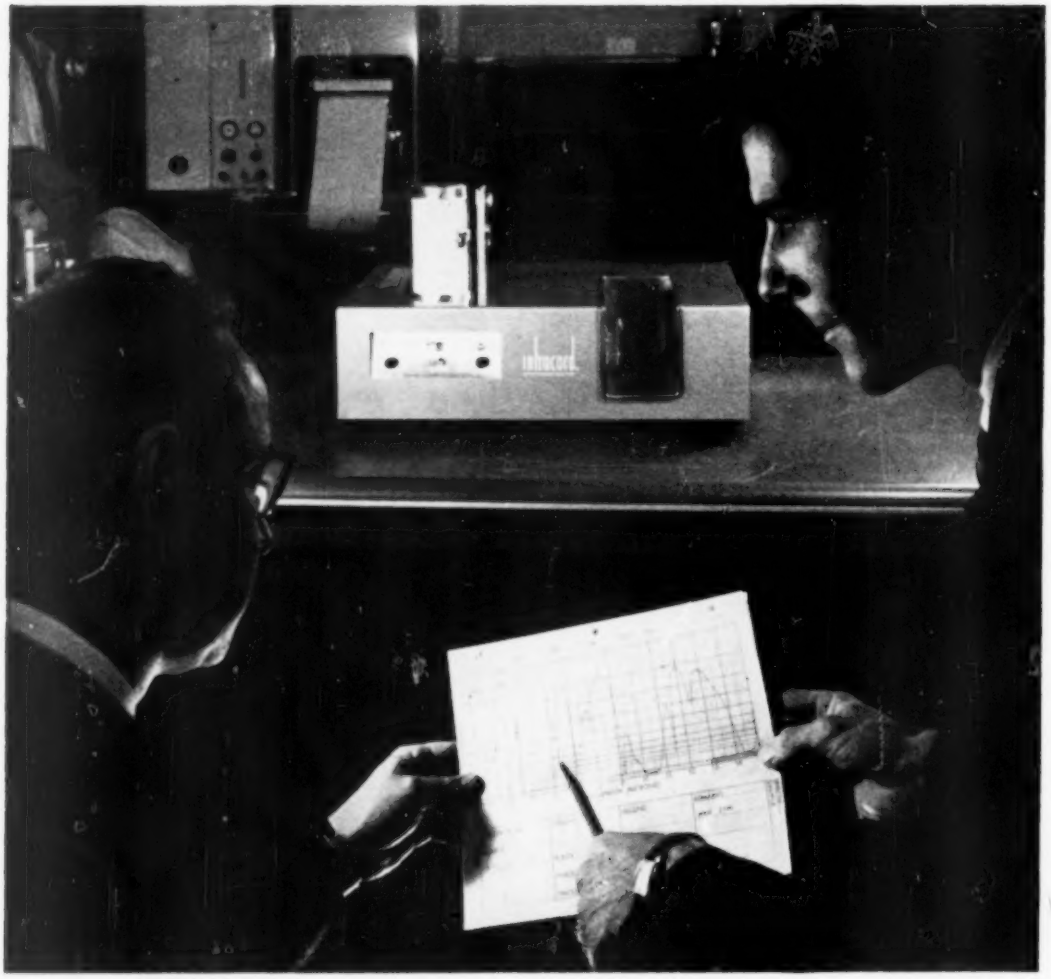

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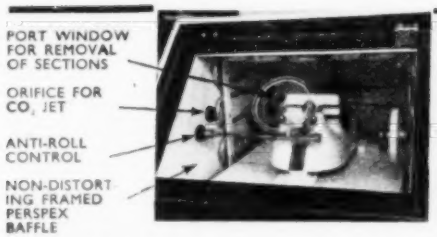

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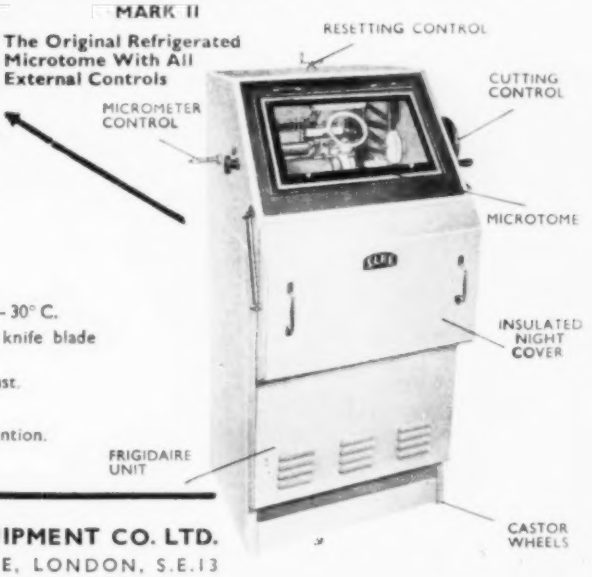

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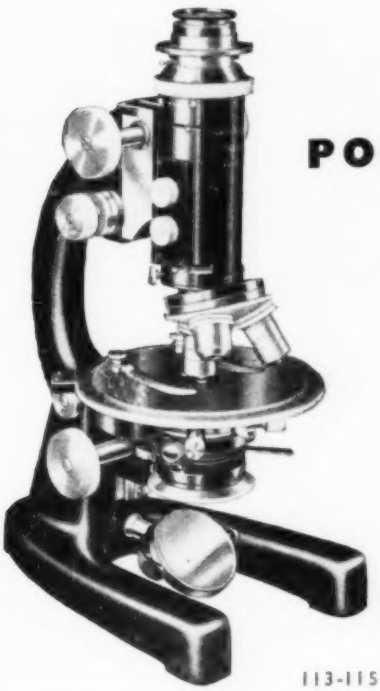

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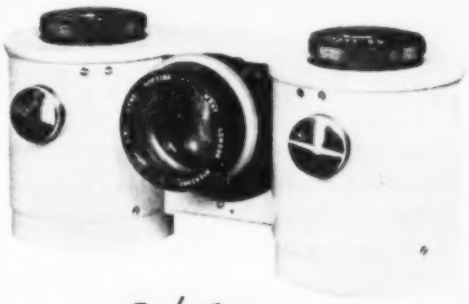

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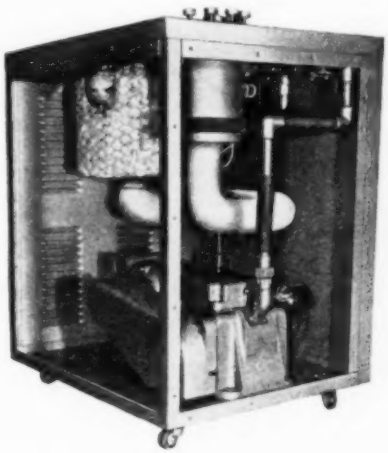

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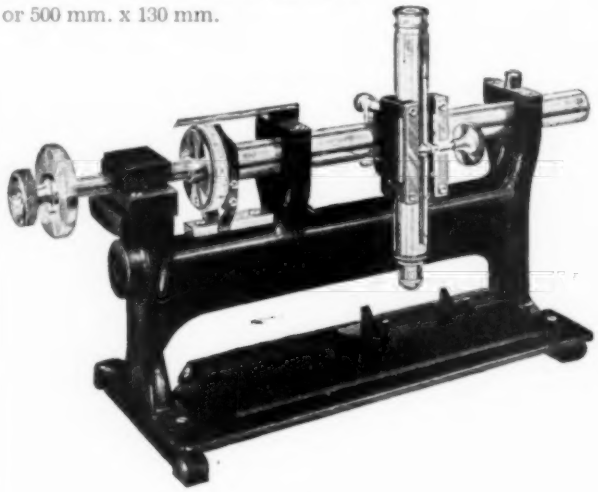

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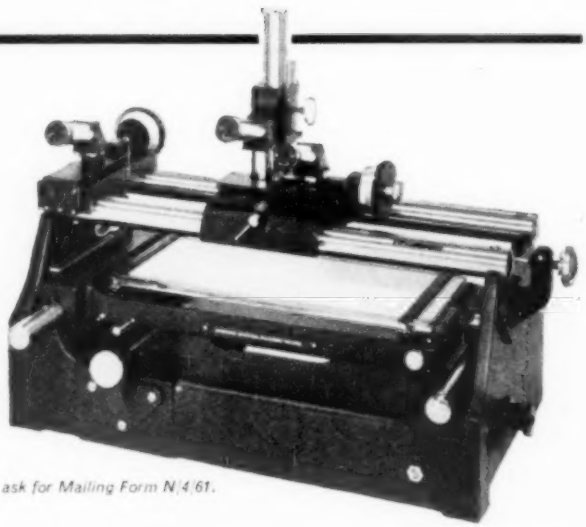

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where λ_- is electron mean free path; f is fraction of energy lost by electron in elastic collision; V_t is voltage across both transition and space-charge zones; V_s is voltage across space-charge zone only; E is field in transition zone, which is assumed approximately constant to aid calculations.

The corresponding deflexion in the amperian direction, y, for an electron moving d_t through the transition zone is given by:

$$y = B\left(\frac{e}{m}\right)^{1/2}\frac{\sqrt{2}}{3}\frac{\lambda_-}{E}(Ed_t + V_s)^{1/2} \qquad (2)$$

where B is transverse magnetic flux density; m is electron mass.

In the physical picture of the model proposed it is implicit that $(Ed_t + V_s)$ must remain approximately constant, in value equal to the first excitation potential of the gas, any variation being merely that required to compensate for variation in the energy loss in elastic collisions.

After the electrons have produced ions at the top of the transition zone by cumulative excitation, the ions drift back to the cathode and condition it so as to give rise to further emission at this new point. Thus the amperian velocity is given by $v = \frac{y}{T}$, where $T = T_1 + T_2$, T_1 being the time for the ions to move from the top of the transition zone to the cathode, and T_2 the time for emission at the new site to become 'established'. Previous experimental results[8] suggest that T_2 is generally greater than T_1. As T_2 would not be expected to vary with magnetic field strength and pressure the arc velocity should be proportional to the deflexion y. Therefore one would expect the velocity to be directly proportional to B, the magnetic flux density, as is in fact observed[2,9]. When the ambient pressure is reduced below atmospheric, Yamamura[9] finds that the velocity decreases only slowly, or not at all, until a critical value $\sim$ 200–400 torrs is attained, following which the velocity falls rapidly to zero on further pressure reduction. Over the range of pressure where v remains almost constant it appears from equation (2) that $\frac{\lambda_-}{E}$ is approximately constant. This is not altogether surprising as the increase in λ_- with decrease of pressure causes $eE\lambda_-$ to increase compared with kT_e (k is Boltzmann's constant, T_e is electron temperature), so that back-diffusion of electrons in the transition region is checked and E correspondingly increases. The process is therefore cumulative. As $(V_s + Ed_t)$ is approximately constant, d_t decreases as E increases, so that the model progressively approaches that given by Ecker for case (*b*) at low pressure, as would be expected.

For satisfactory channelling of the ions to the cathode $eE\lambda_- > kT_e$. At atmospheric pressure, therefore, E cannot be less than about 5×10^3 V./cm. From equation (2) the value of d_t can thus be estimated, and it may be shown that each electron makes a hundred or so collisions before having an exciting collision, at atmospheric pressure. When the number of elastic collisions per electron in the transition zone becomes small, equations (1) and (2) are no longer valid and the model breaks down. A criterion which loosely defines the point at which the model would fail is:

$$d_s + d_t \simeq \lambda_- \qquad (3)$$

Calculations indicate that the relation (3) is satisfied at 300–400 torrs, which is the same region as experiments indicate that the velocity tends rapidly to zero.

Finally, substitution of experimental quantities in equation (2) and the use of measured velocities yield values for T. T_1 may be calculated and this shows values of T_2 which are reasonable in the light of previous observations[8]. It would therefore appear that the proposed model offers a reasonable explanation for amperian arc motion.

It is hoped to publish a more detailed account of this mechanism and confirmatory experimental data elsewhere.

We thank Prof. M. W. Humphrey Davies for his interest and encouragement, and Mr. G. E. Austen of the Electrical Research Association for his help in translating. One of us (P. E. S.) wishes to acknowledge the award of a research fellowship by the Department of Scientific and Industrial Research.

P. E. Secker
A. E. Guile

Department of Electrical Engineering,
Queen Mary College,
London, E.1.

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Variation with Temperature of the Photoelastic Constants of Sodium Chloride

Recently, Bhagavantam and Krishnamurty[1] investigated the variation with temperature of the stress-optical constants $(q_{11}-q_{12})$ and q_{44} of a few alkali halide crystals, using Babinet and Rayleigh compensator methods. In continuation of these investigations, we have now undertaken the study of the variation with temperature of the stress- and strain-optical constants of a number of cubic crystals in the temperature range 30–300° C., for the wavelength 5890 Å. This communication gives the outline of the method and the results obtained in the case of sodium chloride.

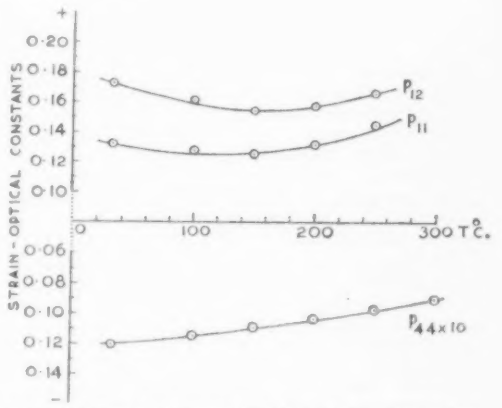

Fig. 1. Variation with temperature of the absolute strain-optical constants of sodium chloride

Table 1

Temperature (° C.)	$-(q_{11}-q_{12})$ (units of 10^{-13} c.g.s.)	$-(p_{11}-p_{12})$	p_{12}/p_{11}	p_{11}	p_{12}	$-q_{44}$ (units of 10^{-13} c.g.s.)	$-p_{44}$
32	1·12	0·041	1·31	0·132	0·172	0·94	0·0120
100	0·99	0·033	1·26	0·128	0·161	0·90	0·0113
150	0·91	0·029	1·23	0·125	0·154	0·87	0·0108
200	0·84	0·025	1·19	0·132	0·157	0·84	0·0103
250	0·78	0·022	1·15	0·145	0·167	0·80	0·0096
300	0·74	0·020	—	—	—	0·76	0·0090

A modified form of Filon's method[2], with a suitable heating arrangement, has been used to measure the stress-optical constants $(q_{11}-q_{12})$ and q_{44} at different temperatures. From these results, using the appropriate elastic constants, the strain-optical constants $(p_{11}-p_{12})$ and p_{44} are evaluated. To determine the absolute strain-optical constants p_{11} and p_{12}, the ratio p_{12}/p_{11} is measured at different temperatures by a modification of the ultrasonic method[3]. Combining the values of p_{12}/p_{11} and $(p_{11}-p_{12})$, the absolute strain-optical constants p_{11} and p_{12} have been evaluated. Table 1 shows the results obtained for sodium chloride. It was possible to measure p_{12}/p_{11} up to only 250° C., as the Hiedemann pattern became very diffuse above this temperature. The variation with temperature of p_{11}, p_{12} and p_{44} is shown graphically in Fig. 1. The elastic constants at different temperatures needed for these calculations are taken from a paper by Hunter and Siegel[4] and the thermo-optical data have been provided by M. A. H. Shareef (private communication). Work with other crystals is in progress and will be published in due course.

K. V. Krishna Rao
V. G. Krishna Murty

Physics Department,
Osmania University,
Hyderabad, 7,
India.

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Intensity Aspects as Determinant of $r_e'-r_e''$ in the Bands of the Lanthanum Oxide (LaO)($B \rightarrow X$) System

An attempt made by Meggers and Wheeler[1] to investigate the rotational analysis of the yellow system of lanthanum oxide did not prove successful, because of the low resolving power of the concave grating used by them. This band system has not yet been subjected to a successful structure analysis, though some attempts are under way[2]. Tawde and Chandratreya[3] have estimated the difference (Δr_e) in the internuclear separations in the levels B and X of this system to be 0·057 Å., mainly from the study of vibrational transition probabilities in relation to asymmetry of the molecules. A later investigation[4] on the vanadium oxide (VO) (green-yellow) system has revealed the validity of revised rotational constants[5]. This was based purely on consideration of the results of the comparative study of the experimental and theoretical transition probabilities, and not on the study of the asymmetry effect on the transition probabilities made by them for the purpose. It occurred to me to establish the Δr_e-value of the yellow system of lanthanum oxide from considerations similar to those in vanadium oxide, so as to enable those engaged in the rotational analysis of this band system to use the value as a check on their determinations.

Chandratreya[6] has derived the experimental transition probabilities of this band system. They are shown in Table 1. His value of the experimental transition probability of the (0,0) band, which is the intense band of the system, is 0·79. Using this value and the mathematical technique of Manneback[7], Δr_e is calculated for the (0,0) band. It is found to be $0{\cdot}0378_2$ Å. This value was checked from two other bands (0,1) and (1,0) and is about $\pm 0{\cdot}004$ Å. on either side. With this value of Δr_e, the Franck-Condon factors of the other bands have been computed and are shown in Table 1. Hutchisson's method[8] has been used to check these values[9].

Table 1

Band v', v''	Experimental	Theoretical $\Delta r_e = 0{\cdot}0378_2$ Å.	Band v', v''	Experimental	Theoretical $\Delta r_e = 0{\cdot}0378_2$ Å.
0,0	0·79	0·79	2,0	0·05	0·02
0,1	0·21	0·18	2,1	0·14	0·32
0,2	0·05	0·03	2,2	0·31	0·24
			2,3	0·40	0·28
1,0	0·16	0·19	2,4	0·08	0·11
1,1	0·57	0·46	3,1	0·07	0·04
1,2	0·31	0·26	3,2	0·26	0·39
1,3	0·05	0·07	3,3	0·27	0·11
			3,4	0·49	0·25

The molecular constants needed for this computation are taken from Herzberg's treatise[10]. As lanthanum oxide is a molecule of considerable astrophysical importance[11], these two sets of transition probabilities will be useful to the astrophysicists. It is found from Table 1 that there is a good agreement of the experimental transition probabilities with the theoretical set calculated with $\Delta r_e = 0{\cdot}0378_2$ Å., though simple harmonic oscillator wave-functions are used in the theoretical calculations. A similar investigation by Tawde and me on the vanadium oxide (green-yellow) system referred to above lends support to such a method of assigning $\Delta r_e \sim 0{\cdot}038$ Å. in the case of B- and X-levels of lanthanum oxide.

I am grateful to Prof. N. R. Tawde for suggesting the problem. I thank the Council of the National Institute of Sciences of India for the award of a post-doctoral senior research fellowship.

N. Sreedhara Murthy

Department of Physics,
Karnatak University,
Dharwar, India.

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Two-dimensional Fourier Transform Technique for analysing Random Structures

In the course of a number of analyses of random interstratification of layers, it has been shown that a one-dimensional Fourier transform can be calculated which gives a clue to the correct sequence of layers[1,2].

This method can readily be generalized to two and three dimensions. Suppose we have scattering material, for example, in the form of layers (this is not an essential feature of the method), and that this can be stacked in two or more ways. Suppose that these manners of stacking are mixed together randomly. The result will be an X-ray diagram which consists partly of sharp spots, and partly of diffuse bands. Viewed in three dimensions, the layers will give rise to a series of regularly packed reciprocal rods. These will have a distribution of intensity along them depending on the structure of the layer, and this distribution will further be modified by the nature of the superposition of layers.

Let us consider any plane in reciprocal space, say the $(h0l)$ plane, where (001) is the basal plane. The intensity function of such a partially random crystal as we are considering will have a strict periodicity in the h direction, but will be non-periodic in the l direction. It is now possible to generalize the one-dimensional Fourier transform which one of us has described[2] into a two-dimensional transform, consisting of an infinite band, periodic in the a direction, and non-repeating in the c direction. This function will have maxima at points corresponding to unit-cell repeat distances which are present in the random crystal. These unit-cell repeat distances will be shown vectorially. Furthermore, 'combination peaks' will show the degree of randomness in the mixture, as has been described for the one-dimensional case[2].

The result of this will be to give a vector diagram showing the nature of the various combinations of translations which occur. Fig. 1 shows such a diagram for random mixtures of (*a*) a 15 Å. spacing of $\frac{1}{2}a$ translation, and a 17½ Å. spacing of $\frac{1}{2}a$ translation; (*b*) a 15 Å. spacing of $\frac{1}{2}a$ translation and a 21 Å. spacing of 0 translation.

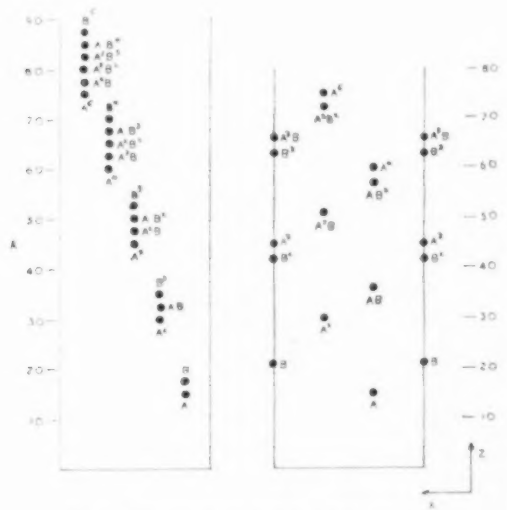

Fig. 1. Theoretical periodograms for two mixtures

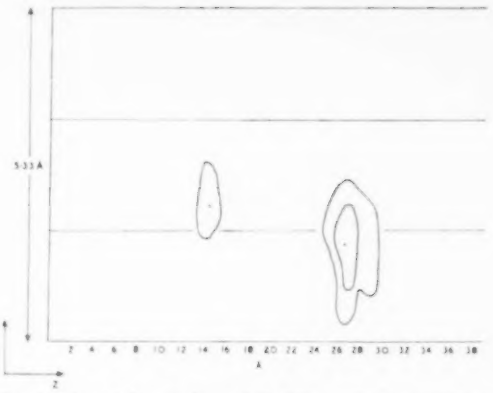

Fig. 2. A periodogram for a $C_6H_{13}NH_2$-vermiculite complex

Fig. 2 shows an actual example of a Fourier transform calculated by this method. It is for a vermiculite complexed with $C_6H_{13}NH_2$. It shows peaks at 14 Å. and 26·5 Å., both corresponding to translation of about $\frac{1}{2}a$.

In contrast to an ordinary Fourier synthesis, a diagram of this sort gives the *periodicities* associated with the crystal, and it may therefore conveniently be called a *periodogram*.

Douglas M. C. MacEwan
H. H. Sutherland

Carnegie Laboratory of Physics,
Queen's College, Dundee.

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METALLURGY

Creep of Metals under Simple Shear

In a paper published last year[1], we showed with polycrystalline lead, subjected to a constant simple shear stress, that the $t^{1/3}$ law of creep held very closely within a certain range of strain, the average error being about 0·25 per cent of the range in question. We recorded, however, that for low strains, below about 0·03 with a particular lead, the law was not obeyed, the strain varying more rapidly than was indicated by the law. At high strains, too, the law fails owing to recrystallization, but to comment on that is not the object of the present communication.

Using a more sensitive recording device, we have since found that, for the lower strains in question, the strain under simple shear stress varies precisely as $t^{1/2}$. Thus with a lead for which the $t^{1/3}$ regime begins at a strain of 0·035 in the range of strain from 0·012 to 0·035, the $t^{1/2}$ law, fitted by least squares, holds with an average error of 0·25 per cent of the range, which is about the error of observation.

This $t^{1/2}$ law has been confirmed with leads differing in the small amounts of foreign metal contained, and with cadmium. For the creep under reversed stress, which can be accurately measured by the

method in question, the $t^{1/2}$ law also holds within a definite range.

Mr. D. B. Gilding, working under the supervision of the senior of us with the method described in *Nature* last year[2], has confirmed the validity of the $t^{1/2}$ law over a range of small strains with lead and with cadmium.

There is evidence that at still lower strains a different power law, namely $t^{2/3}$, is valid.

Experiments are proceeding with the object of determining the glide mechanism corresponding to the different stages, so as to establish a mechanical explanation of the general creep behaviour.

E. N. da C. Andrade
K. H. Jolliffe

Department of Metallurgy,
Imperial College of Science and Technology,
London, S.W.7.

[1] Andrade, E. N. da C., and Jolliffe, K. H., *Proc. Roy. Soc.*, A, **254**, 291 (1960).
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Cleavage Fracture Initiation in Notched Impact Tests of Mild Steel

Many experimental observations have confirmed that brittle fracture in steel consists mainly of cleavages on the cube planes of ferrite crystals in the aggregate, with ductile fractures of the bridges formed between them. Important doubts have been expressed as to a cleavage being initiated within a crystal until the intervention of a discrete, inelastic local displacement, which might act as a trigger. Several hypotheses have arisen as to the nature of the trigger mechanism, principally involving slip and twinning. A well-known hypothesis, due to Cottrell[1], involves the intersection of two mutually perpendicular slip bands to form a strain incompatibility giving rise in turn to a void, from which cleavage may nucleate. To the best of our knowledge, the operation of this mechanism has not before been observed in steel.

Our experiments have been undertaken to explore further the nucleation of cleavage fracture in notched specimens, for which we have modified the Charpy impact test. Our objective has been to arrest the fracture as quickly as possible after initiation, in order to study the relative positions of the two fractured surfaces before they separate, using a method made known to us by Kasatkin[2]. In our development of this method, the specimen is deformed by impact at the full speed of the machine, until further bending is stopped by a surrounding rigid frame which accepts the remaining energy of the blow and transmits it to blocks of balsa wood which are permitted to be crushed. In order to secure early arrests, it has been found convenient to notch the specimens to 5 mm. depth, using a standard milling cutter of 0·25 mm. root radius, and to preform the specimens by about 2° of slowly applied bending in the reverse direction to assist crack initiation in the manner demonstrated by Mylonas[3]. We have used specimens of annealed mild-steel, bent by impact to angles between 1° and 5°, and the cracking has been observed on etched microsections taken at mid-thickness. At our testing temperature of 0° C. a completely fractured specimen of standard size shows an energy absorption of 5 ft. lb. and 95 per cent projected area of crystallinity in the fractured surface.

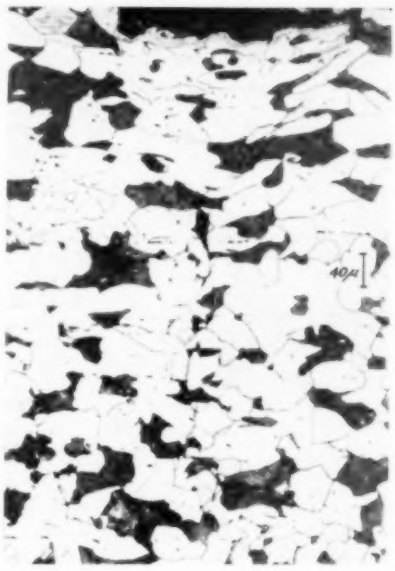

Fig. 1

The accompanying photomicrograph (Fig. 1) shows a fracture arrested at a very early stage (× 125). A significant feature is the void existing at the junction of terminating planes of heavy slip, extending from the flanks of the original notch. The cleavage fracture appears to extend from the void towards the neutral axis of the specimen, and away from the heavily deformed area. Isolated zones of twinning accompany the main cleavage fracture, but the investigation has yet contributed no evidence to distinguish their part in the process. There are isolated cleavage micro-cracks in advance of the main fracture front.

The initiation mechanism exposed in this specimen appears to correspond with Cottrell's hypothesis, but on a polycrystalline rather than single crystal scale.

The work is to be reported in detail soon.

J. W. Davies
A. A. Wells

British Welding Research Association,
Abington Hall,
Cambridge.

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CHEMICAL ENGINEERING

Polymers of Carbon Dioxide

Polymeric ions of the form $(CO_2)_2^+$, $(CO_2)_3^+$, ... $(CO_2)_{22}^+$ have been observed in the mass spectrum of carbon dioxide. These may be produced from corresponding molecules in carbon dioxide gas.

The mass spectrometer in which these ions were observed was originally built for investigating free radicals in gases at high pressures. A molecular-beam system is used for transferring the gas from a reservoir to the ion source so that reactive species are not destroyed by wall collisions. Gas molecules pass through a 0·00062-in. diameter orifice and then

through a series of larger orifices which define the molecular beam and which are separated by pumping chambers. The molecular beam passes directly into the ion source where ions are formed in the usual way by electron bombardment; the spectrometer itself is a conventional magnetic sector field instrument. Further details of the apparatus are given elsewhere[1].

When carbon dioxide (commercial grade, from a cylinder), at a reservoir pressure of up to 4,000 mm. mercury and at room temperature, is examined with this system, the mass spectrum is found to contain ions corresponding with the groups $(CO_2)_n^+$. Relative intensities of ions CO_2^+, $(CO_2)_2^+$, ..., $(CO_2)_{23}^+$ for a pressure of 3,800 mm. mercury (5·0 atm.) are given in Fig. 1.

Ion intensities change very rapidly with reservoir pressure, as shown in Fig. 2 for $(CO_2)_2^+$. In this case the experimental points follow the power law: $I_2 = K_2 P^{2\cdot85}$, where I_2 is the $(CO_2)_2^+$ ion intensity, P is the reservoir gas pressure, K_2 is a constant. Similar power laws are followed by ion intensities of larger polymers, namely:

$$I_3 = K_3 P^{3\cdot5} \text{ for } (CO_2)_3^+$$
$$\text{and} \qquad I_4 = K_4 P^{3\cdot1} \text{ for } (CO_2)_4^+$$

For the polymers larger than $(CO_2)_4^+$, the change in ion intensity with pressure is too rapid to permit even approximate measurements.

There are three possible sources for these polymeric ions: (1) They are formed in the mass spectrometer itself, either by ion-molecule reaction or some other process. (2) Polymeric molecules are formed during the expansion of the gas from the reservoir into the molecular-beam system. (3) Polymeric molecules are present in carbon dioxide gas.

The first possibility has been investigated in detail; although the evidence is not completely conclusive, it seems reasonably certain that the source of the polymers is not in the mass spectrometer. There is no evidence to indicate whether the second possibility is the cause or not; however, it seems unlikely, since an expansion involves (on average at least) the separation of adjacent molecules. Cooling of the bulk gas as a result of the Joule–Thompson effect is less than 6° C.[2] and would therefore seem to be negligible.

The third possibility, that polymeric molecules are always present in carbon dioxide, thus seems to be the most probable in the light of existing evidence.

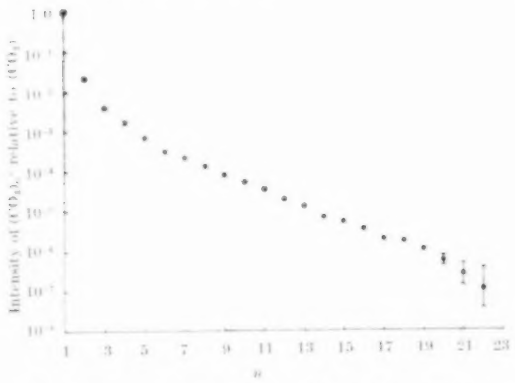

Fig. 1. Measured ion intensities for polymeric ions $(CO_2)_2^+$ — $(CO_2)_{23}^+$. Reservoir pressure, 3,800 mm. mercury

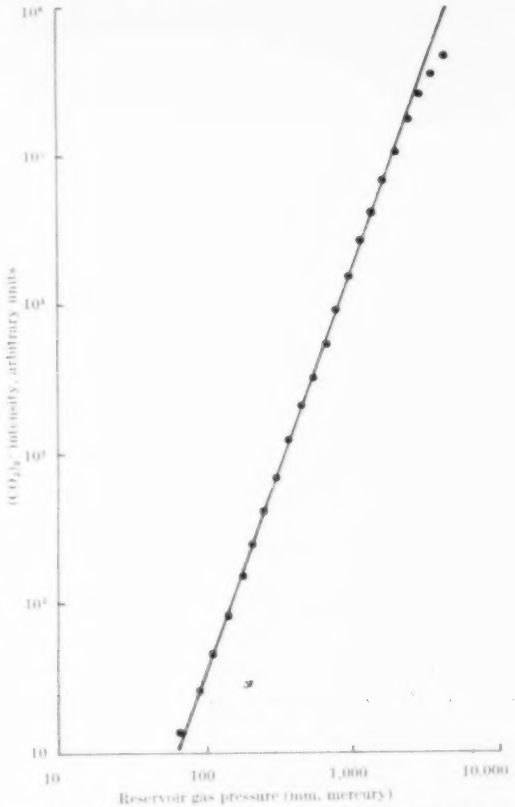

Fig. 2. Variation of $(CO_2)_2^+$ ion intensity with reservoir pressure. ●, Experimental points; —, $I_2 = K_2 P^{2\cdot85}$

Measurements at different temperatures might help in locating the source of the polymers; investigation of other gases would also be interesting.

This communication was submitted for publication by permission of Sir William Cook, managing director, and Dr. H. Kronberger, deputy managing director, of the U.K. Atomic Energy Authority (Development and Engineering Group).

P. G. Bentley

United Kingdom Atomic Energy Authority
(Development and Engineering Group),
Reactor Technology Branch,
Capenhurst, Chester.

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Bubble Formation at an Orifice in a Fluidized Bed

When a gas is passed through a bed of solid particles supported by a porous distributor at a flow-rate sufficient to fluidize the bed, gas bubbles can usually be seen travelling up through the bed and breaking surface at the top. The properties of bubbles in fluidized beds have become the subject of considerable interest recently for the information

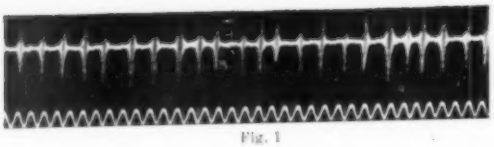

Fig. 1

their study provides on the mechanics of fluidization, and also for the part gas bubbles play in gas-solids coming into contact in fluidized beds. How gas bubbles form in fluidized beds is, however, largely unknown.

It has been shown[1,2] that the properties of gas bubbles in fluidized beds can often be described in terms of the properties of spherical-cap gas bubbles in inviscid liquids of zero surface tension[3]. The bubble and particulate (or dense) phases of a fluidized bed appear to be analogous to the gas and liquid phases in a two-phase system. A study of the formation of a gas bubble at an orifice in an inviscid liquid has recently been published[4] in which it is shown from first principles that the volume of bubble (V ml.) formed at an orifice is given by :

$$V = 1{\cdot}378\, G^{1{\cdot}2}/g^{0{\cdot}6} \qquad (1)$$

where G (ml./sec.) is a constant gas flow-rate through the orifice and g is the acceleration of gravity. In the same investigation the relationship between bubble volume and gas flow-rate through the orifice was investigated experimentally, and the results were found to be in good agreement with equation (1). Some experiments are now described in which a capacitance technique was used to determine the frequency of bubble formation at an orifice in a fluidized bed. The gas flow-rate through the orifice was known and hence the bubble volume could be calculated from the frequency. It has been found that these results may also be interpreted by equation (1), which is new evidence to support the analogy already found between two-phase systems and fluidized beds. It is hoped that these experiments will throw light on the mode of bubble formation in a fluidized bed supported by a distributor made up of orifices; and also provide information on the initial size of a bubble in a fluidized bed.

The apparatus consisted of a 6-in. diameter tube in which a bed of particles was supported by a filter cloth distributor. Two sets of experiments, using sand (mean diameter 0·01 cm.) and alumina catalyst (mean diameter 0·0057 cm.), were carried out with air as the fluidizing gas. An independent stream of air at a known flow-rate was passed into the bed through a narrow injector tube, the end of which was arranged in the centre of the bed about one-third the way up from the distributor. The technique for measuring the frequency of bubble formation from the orifice at the end of the injector tube was to record the change in capacitance between a probe placed at the orifice and a probe about 3 cm. away from it in the fluidized bed. The diameters of the injector tube and the orifice were identical. A Fielden type *PM2* proximity meter coupled to an oscilloscope was used to determine the changes in capacitance as bubbles were formed, grow, and detached from the orifice. Fig. 1 shows the output from the proximity meter for an experiment using catalyst particles, together with the 50 c./sec. trace. In this experiment the frequency of bubble formation from an orifice of 0·125 cm. diameter was approximately 32/sec. Fig. 2 shows a plot of the bubble volume against the flow-rate of air through the orifice compiled from about 30 separate experiments using either sand or catalyst particles. The complete line in the figure is a plot of the theoretical relationship between bubble volume and gas flow-rate given by equation (1). It can be seen that there is good agreement between the experimental results and the theoretical curve for flows up to about 10 ml./sec. It is noteworthy that equation (1) was also found to become inaccurate at high flow-rates in the work on air and water[4]. In the fluidized bed experiments it is considered that this inaccuracy is due in part to the formation of 'double bubbles'. Within the range of the experiments carried out so far with various sizes of orifice, the bubble frequency appears to be largely independent of bed height, the main air flow-rate to the fluidized bed, and the nature and size of the particles.

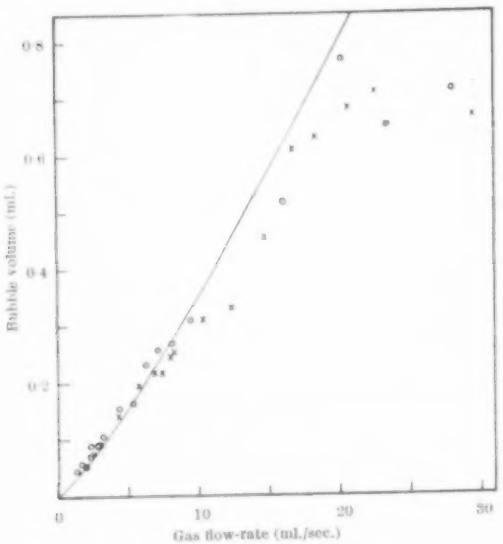

Fig. 2. Graph of bubble volume versus gas flow-rate. ○, Sand in air; ×, catalyst in air; — $1{\cdot}378\, G^{1{\cdot}2}/g^{0{\cdot}6}$

D. Harrison
L. S. Leung

Department of Chemical Engineering,
Pembroke Street, Cambridge.

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CHEMISTRY

Radiometric Precipitation in Filter Paper : a Rapid Method of Micro-analysis

A RADIOACTIVE material can usually be detected and quantitatively measured by simple instrumental methods at levels much below those accessible to other analytical techniques. In theory, if an inactive material reacts quantitatively with the active material and the compound formed can be separated from the unreacted activity, then the inactive material also can be analysed at the same low levels. With this in mind, several workers[1,2] have reviewed the theory of radiometric analysis and considerable progress has

been made in its application[3-6]. In most cases, however, the difficulty of achieving clean phase separations at μgm.-levels is very great. In addition, to achieve reasonable precision and speed, it has nearly always been necessary to count the excess of unreacted activity rather than the compound formed; a procedure which reduces greatly the sensitivity of the method.

Using filter paper as a supporting medium and extending methods which have been found of value in spot tests[7,8] and paper chromatography[9,10], a rapid and simple method of micro-analysis has been developed which overcomes most of these difficulties. It consists in forming a precipitate from the active and inactive materials in the pores of filter paper and washing the paper to remove unreacted activity. The paper disk is then counted along with disks prepared in an identical manner from calibrating solutions. The method was used as follows for the determination of beryllium with a phosphate solution containing phosphorus-32.

Disks of Whatman 42 filter paper of 2 cm. diameter were numbered in pencil and arranged in rows on a glass sheet. By means of a pipette, the centre of each circle was spotted with 0·05 ml. of different beryllium solutions of known strength. After drying *in situ* at 100° C., the paper disks were transferred to about 100 ml. of 0·3 *M* diammonium hydrogen phosphate buffered at about *p*H 5·5 with sodium acetate and giving about 160,000 c.p.m. of phosphorus-32 per ml. The solution was stirred intermittently for 15 min., following which the active solution was poured off (for re-use). The paper disks were rinsed twice with demineralized water and washed for 30 min. by passing a stream of tap water into the beaker. The disks were then transferred to a large sheet of absorbent paper, dried under an infra-red lamp and counted in aluminium planchets with an end window Geiger counter. Results are given in Table 1.

Table 1

Strength of Be^{2+} solution	0·000 *N*	0·025 *N*	0·050 *N*	0·100 *N*	0·200 *N*
Counts/min./disk	72	280	549	936	1,761

These points plot to a good straight line. Good calibration plots of slightly lower precision were also obtained when 0·10 ml. or 0·01 ml. of the beryllium solutions was transferred to the filter paper instead of the 0·05 ml. used for the results quoted. The precision of a determination in the concentration-range examined would be about 2 per cent but would depend on the nature and amount of impurities and on the care taken to ensure that all the paper disks are treated in an identical manner.

The method was also applicable to the determination of magnesium by precipitation of $MgNH_4{}^{32}PO_4$ instead of $BeNH_4{}^{32}PO_4$. The interference of magnesium in the determination of beryllium could be prevented by the use of ethylenediamine tetraacetic acid in the precipitating solution. There are also indications that it will be possible to operate the method in reverse form using an isotope dilution procedure. Thus, if the centre of the paper disks is spotted with 0·05 ml. of the same inactive diammonium hydrogen phosphate solution and the disks, after drying, are transferred to beryllium solutions containing the isotope beryllium-7 at different specific activities, then the activity taken up by the paper is a reasonable function of the specific activity of the beryllium in solution provided that the total concentrations of beryllium do not vary too widely.

A method to determine chloride ion by a similar technique (by immersing the chloride-impregnated paper disks in a nitric acid solution of ^{110m}Ag) gave a reasonable calibration curve when less than about 30 μgm. of Cl^- was present on the paper, but the results were anomalous at higher levels. These anomalies are thought to be due to a change in the physical form of the precipitate on the paper when certain concentration-levels are exceeded, which results in a larger fraction being removed by the standard washing technique. Further study of the factors affecting the nature of silver precipitation in filter paper will undoubtedly be very profitable since this useful isotope can form precipitates with a large number of organic compounds as well as many inorganic anions.

M. Thackray

Australian Atomic Energy Commission,
Research Establishment,
Lucas Heights,
New South Wales.

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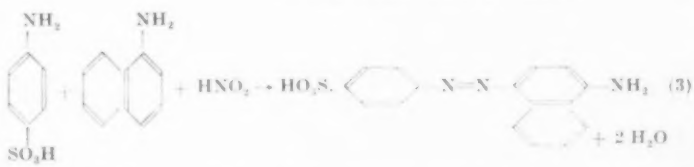
Continuous Determination of Traces of Nitric Oxide

All known methods[1] for the determination of traces of nitric oxide in coke oven gas and air make use of the oxidation, both by means of liquid-phase (permanganate) and gas-phase (ozone) oxidation, to nitrogen dioxide and the subsequent absorption and reaction in the Griess-Ilosvay reagent followed by colorimetric measurement of the azo dye. Calibration can be carried out using standard sodium nitrite solution and assuming the following reactions:

$$2\,NO + O_2 \rightarrow 2\,NO_2 \qquad (1)$$

$$2\,NO_2 + H_2O \rightarrow HNO_2 + HNO_3 \qquad (2)$$



(3)

It has been pointed out[1,2], however, that the analysis is affected by the non-stoichiometric character of this reaction sequence. Consequently, the reliability of the determination depends on the standardization procedure.

In order to meet the requirements for a continuous recording of traces of nitric oxide in coke oven gas and air, we have envisaged the possibility of a fast

Table 1. Photo-oxidation of Nitric Oxide in a Nitrogen–Oxygen Mixture (0·3 per cent Oxygen) with Variable Amounts of 1,3-Butadiene
(H.P.K. mercury lamp (without filter), contact time in quartz tube 5 sec.)

1,3-Butadiene (per cent by vol.)	Nitric oxide introduced* (m.mol.)	Nitrous acid in first spiral washer with Griess-reagent (m.mol.)	Nitrous acid in second spiral washer after preceding oxidation with $KMnO_4$ (m.mol.)
0·0	$2·0 \times 10^{-3}$	$0·0 \times 10^{-3}$	
0·001	$2·0 \times 10^{-3}$	$0·32 \times 10^{-3}$	$0·47 \times 10^{-3}$
0·01	$2·0 \times 10^{-3}$	$1·06 \times 10^{-3}$	$0·24 \times 10^{-3}$
0·05	$2·0 \times 10^{-3}$	$1·01 \times 10^{-3}$	$0·07 \times 10^{-3}$
0·1	$2·0 \times 10^{-3}$	$1·01 \times 10^{-3}$	$0·04 \times 10^{-3}$

* Concentration about 1 p.p.m.

and reliable determination which approaches as closely as possible the reaction sequence given above.

It has already been pointed out by Fullweiler[3] that the oxidation of nitric oxide to nitrogen dioxide is accelerated by dienes (an instrument based on this principle is marketed by the Rubicon Co.). However, owing to the still relatively slow rate of oxidation, this method cannot be applied for the recording of rapid changes in concentration.

We have found (patent applied for) that a fast (contact time of 5 sec.) oxidation of traces of nitric oxide can be effected by irradiation with a high-pressure mercury vapour lamp. From a preliminary investigation on the reaction mechanism it appeared that the photo-oxidation of nitric oxide occurs only in the presence of dienes. In addition it was found that with 1,3-butadiene the effective wave-length region is below 2300 A. Therefore it seems likely that the first step in the photo-oxidation of nitric oxide comprises the formation of an excited butadiene molecule, which persists long enough[4] to react with oxygen to a peroxide.

The latter may undergo reaction, through a chain mechanism[5], with nitric oxide and oxygen to nitrogen dioxide:

$$D\,(\text{diene}) + h\nu \longrightarrow D^* \qquad (4)$$

$$D^* + O_2 \longrightarrow DO_2 \qquad (4)$$

$$DO_2 + 2\,(NO) \longrightarrow DO_2\,(NO)_2 \qquad (5)$$

$$DO_2\,(NO)_2 + O_2 \longrightarrow DO_2 + 2\,NO_2 \qquad (6)$$

Thus, as a result of the formation of an excited diene molecule, the normal induction period of the oxidation of nitric oxide is decreased appreciably.

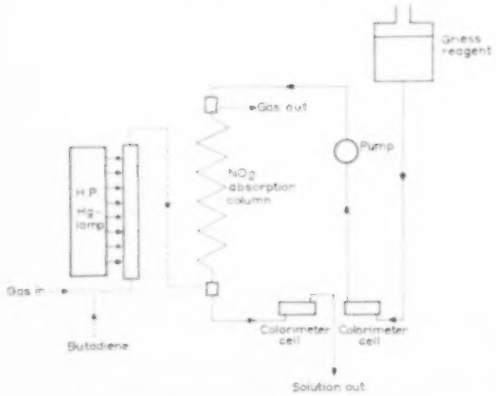


Fig. 1. Schematic diagram of nitric oxide recorder

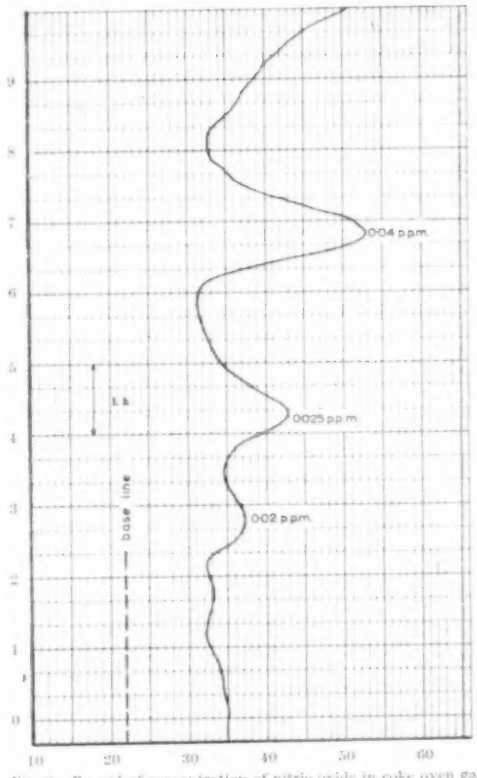


Fig. 2. Record of concentration of nitric oxide in coke oven gas (8 scale divisions = 0·01 p.p.m. oxide)

Some results of the oxidation of nitric oxide in a nitrogen–oxygen mixture with variable amounts of 1,3-butadiene are given in Table 1.

It appears that for butadiene concentrations of 0·05 per cent and higher the stoichiometry of equations 1–3 is satisfied.

A continuous nitric oxide recorder was developed based on the photo-oxidation of nitric oxide and the subsequent absorption and reaction in a spiral washer with Griess-Ilosvay reagent followed by colorimetric measurement by means of a flow type colorimeter[6]. A block diagram of the instrument is given in Fig. 1.

The nitric oxide recorder is applied for the continuous determination of nitric oxide in coke oven gas. A typical record is given in Fig. 2, in which 0·01 p.p.m. corresponds with eight scale divisions.

Finally, the method has also been applied to examination of air pollution. In this case additional 1,3-butadiene, which is already present in sufficient amount in coke oven gas, must be supplied to the air stream.

C. Bokhoven
P. H. Tommassen

Dutch State Mines,
Central Laboratory,
Geleen, The Netherlands.

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Distribution of Oxygen in a Vitrinite and its Extraction Products

A VITRINITE (petrographic purity: 99 per cent; analysis (moisture- and ash-free): 83·9 C; 5·5 H; 8·0 O; 1·4 N per cent; 1·2 per cent S by difference) was extracted with pyridine, the pyridine-soluble part with benzene, and this extract finally with petroleum ether (boiling point 40–60° C.). The ratio of material to solvent was 10 gm./litre in all cases. Each extraction was carried out in boiling solvent of analytical purity, for a period of 24 hr. with efficient stirring and under purified nitrogen. Exhaustive extraction was thus achieved at each step. A 25 per cent yield was obtained for the pyridine-soluble fraction, which could itself be extracted with benzene to the extent of 20 per cent. The petroleum ether extract represented 40 per cent of the benzene-soluble part. The former was washed further with sodium carbonate, sodium hydroxide and hydrochloric acid to yield 96 per cent of a 'neutral oil'.

The content of hydroxyl groups in vitrinite and its extraction products was determined as described previously[1], with the exception of the benzene-soluble fraction and those derived from it, in which it was better to use a method developed for asphaltic bitumens[2]. The amount of quinone oxygen was measured in the pyridine-soluble and derived fractions by means of an analytical adaptation[3] of quinone reduction with copper and hydrogen sulphide[4].

The results are summarized in Table 1. The first column gives the content of oxygen, determined moisture- and ash-free. In the petroleum ether-soluble fraction and the 'neutral oil' there is no ash, but an accurate determination of moisture according to the standard methods used for coal products was not possible on account of the relative volatility of the samples. Therefore, in these cases the analytical data for total oxygen must be considered as maximum values. In the second column (percentage hydroxyl oxygen) the small value reported for the petroleum ether-soluble fraction could not be determined with accuracy, but is certainly correct as an order of magnitude, as can also be ascertained from the near infra-red absorption at about 1·42μ. From the third column (percentage quinone oxygen), it can be seen that the benzene-insoluble fraction is the last in the series to contain quinone oxygen in detectable quantity.

Taking into account that in bituminous coals oxygen is present essentially in the form of hydroxyl groups, quinones, and as 'non-reactive'[5], the results in column 4 show that 'non-reactive' oxygen, calculated by the difference, $O_{total} - (O_{OH} + O_{quin.})$, has a remarkably constant value, of about 2·8 per cent, in all fractions where it follows directly from experimental results. Assuming that this value holds true also for the pyridine-insoluble fraction and for vitrinite itself, their quinone oxygen content can be estimated (see Table 1, column 3, results in square brackets). Considering the experimental errors made, the results obtained fit fairly well in the whole scheme for oxygen distribution in the various fractions.

Trends observed in Table 1 are significant. In each extraction step a disproportionation of hydroxyl groups occurs which favours the insoluble residue. This concentration of polar groups is even more marked with respect to quinones. The above observations can certainly be correlated with the change of polarizability in the solvent series. Further, it may be noted that the ratio of hydroxyl to total oxygen remains remarkably constant down to the petroleum ether-insoluble component. On the other hand, the 'non-reactive' oxygen behaves quite differently, since it remains practically constant in amount from the pyridine-soluble extract down to the neutral oil and should be taken into account as a structural parameter[6].

Table 1. DISTRIBUTION OF OXYGEN IN A VITRINITE (83·9 PER CENT CARBON) AND ITS EXTRACTION PRODUCTS

Sample	Percentage oxygen (moist.-, ash-free)	Percentage hydroxyl oxygen	Percentage quinone oxygen	Percentage non-reactive oxygen (by difference)
Vitrinite	8·0	4·2	[1·0]	[2·8]
Pyridine-insoluble	9·0	4·5	[1·7]	[2·8]
Pyridine-soluble	7·2	3·3	1·0–1·2	2·9–2·7
Benzene-insoluble	8·5	3·7	1·6–1·8	2·8–3·0
Benzene-soluble	4·4	1·8	—	2·6
Petroleum ether-insoluble	5·3	2·5	—	2·8
Petroleum ether-soluble	max. 3·1	(0·5)	—	(2·6)
'Neutral oil'	max. 3·1	—	—	3·1

Experiments have been initiated in this laboratory to investigate the principal nature of this 'non-reactive' oxygen by chemical means. The infra-red spectrum of the neutral oil is sufficiently specific to show clearly a band at 8·35μ (1,198 cm.$^{-1}$) which can be attributed to the antisymmetrical stretching mode of a C—O—C group in which at least one of the carbon atoms is part of an aromatic ring[7]. Thus, making the assumption that the 'non-reactive' oxygen is mainly related to at least partly aromatic ether structures, it seemed worth while to attempt cleavage of these groups with sodium in liquid ammonia[8]. Results so far obtained on the petroleum-insoluble fraction, the neutral oil, and one of its chromatographic fractions (2·5 per cent oxygen) have shown that ether cleavage, indeed, occurs under the conditions of Birch reduction.

The principal change in the infra-red is a new absorption band in the 2·9μ (3,450 cm.$^{-1}$) region due to —OH stretching, accompanied by sharply reduced intensity of the 8·35μ band. After acetylation, the reduced samples show no OH absorption but intense bands at 5·69μ (1,760 cm.$^{-1}$), at 8·31μ (1,205 cm.$^{-1}$) and increased intensity at 7·26μ (1,375 cm.$^{-1}$), which leads to the conclusion that phenolic groups have been acetylated; a further proof that ether oxygen originally present was linked at least on one side to an aromatic system.

The investigation, part of which has been described here, was supported in this laboratory by the Union Carbide Corporation, New York, to which we are grateful for permission to publish the results.

A. HALLEUX
S. DELAVARENNE
H. TSCHAMLER

European Research Associates, s.a.,
95 rue Gatti de Gamond,
Brussels.

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Rate of Oxidation of Ferrohæmoglobin by Ferricyanide Ions

The iron atom in hæmoglobin is part of an octahedral structure with four bonds in a plane to the nitrogen atoms of the pyrrole rings, the fifth bond directly to the globin (probably through the nitrogen atom of the imidazole ring of histidine) and the sixth bond to a water molecule[1]. Recent X-ray diffraction studies have shown that the four hæm-groups are situated on the surface of the hæmoglobin in pockets formed by folds in the polypeptide chains[2]. St. George and Pauling[3] have suggested that in aqueous solutions the folds in the polypeptide chains interfere with the binding of tertiary butyl *iso*cyanide to the hæm group. In an attempt to obtain further information concerning the effect of the environment of the hæm group on the chemical properties of the iron, we have measured the rate of oxidation of ferrohæmoglobin by ferricyanide ions, and compared this rate with that of oxidation-reduction reactions between various iron compounds.

Oxyhæmoglobin was obtained from freshly drawn human blood. About 30 ml. of blood was added to an anticoagulant medium containing acid citrate and dextrose. This was then centrifuged to separate the red cells, which were washed three times with 0·85 per cent saline solution. The red cells were then hæmolysed by adding 1·2 vol. distilled water and 0·2 vol. toluene and gently shaken. The toluene layer was separated from the aqueous layer, which was then centrifuged. The oxyhæmoglobin in the aqueous layer was estimated spectrophotometrically[4]. The oxyhæmoglobin was converted to ferrohæmoglobin by repeated evacuation and equilibration with nitrogen.

The rate of the ferrohæmoglobin–ferricyanide reaction was measured using the rapid-flow apparatus which has been previously described[5]. The reaction was investigated in a phosphate buffer with a *p*H of 6·0 and an ionic strength of 0·10. There is evidence that, at this *p*H, ferricyanide ions oxidize only the hæm group and leave the globin unchanged[6]. Second-order kinetics were observed. The rate constant for the oxidation of the first hæm group was found to be $7{\cdot}0 \pm 0{\cdot}5 \times 10^4$ l. mole^{-1} sec.$^{-1}$ at 25·0° C. with the concentration of the ferrohæmoglobin solution expressed in terms of its hæm content (mol. wt. = 17,000). Attempts to study the rate of oxidation of ferrohæmoglobin by the *tris*-(2,2′-dipyridine) complexes of osmium(III) and ruthenium(III) were unsuccessful, for these oxidizing agents reacted with the globin in addition to oxidizing the hæm-groups.

The ferrohæmoglobin–ferricyanide reaction is compared with oxidation-reduction reactions between various iron compounds in Table 1. This table also includes the products of the charges of the various reactants and the standard free-energy changes of the reactions calculated from the formal oxidation potentials of the appropriate couples[7,8].

It is apparent from Table 1 that the ferrohæmoglobin–ferricyanide reaction proceeds much slower than reactions (5) and (6). This is somewhat surprising in view of the more favourable standard free-energy change of the ferrohæmoglobin–ferricyanide reaction[7,9]. Moreover, the iron atoms in ferrohæmoglobin are uncharged and unless there are high negative charges on the neighbouring groups, the work required to bring the ferricyanide ion close to an iron atom in ferrohæmoglobin will be less than that required to bring the similarly charged ions together in reactions (5) and (6). Provided we neglect any effects due to the differences in the structures and solvations of the various reactants, we may estimate a lower limit for the rate of reaction (3) from the rates of reactions (2) and (4). Assuming that the rates of reactions (2), (3) and (4) are determined solely by the amount of work required to bring the reactants together, the rate constant of reaction (3) should be somewhat larger than the geometric mean of the rate constants of (2) and (4). This estimate will be further increased if in addition we consider the relative standard free-energy changes of reactions (2), (3) and (4). These considerations lead to an estimate of about 10^6 l. mole^{-1} sec.$^{-1}$ for the lower limit of the rate constant of reaction (3). It is apparent from Table 1 that the rate constant of the ferrohæmoglobin–ferricyanide reaction is smaller than this value.

Table 1. Oxidation-Reduction Reactions between Various Iron Complexes at 25° C.

	Oxidizing agent[a]	Reducing agent[a]	Z_1Z_2	ΔG° kcal. mole^{-1}	k l. mole^{-1} sec.$^{-1}$
(1)	$Fe(H_2O)_6^{3+}$	$Fe(H_2O)_6^{2+}$	+ 6	0	4[b]
(2)	$Fe(CN)_6^{3-}$	$Fe(CN)_6^{4-}$	+ 12	0	1×10^3 [c,d]
(3)	$Fe(CN)_6^{3-}$	$Hb(H_2O)$	0	− 6·2	7×10^4
(4)	$Fe(phen)_3^{3+}$	$Fe(CN)_6^{4-}$	− 12	− 5·3	$> 10^{8}$[e]
(5)	$Fe(d\text{-}dipy)_3^{3+}$	$Fe(t\text{-}phen)_3^{2+}$	+ 6	− 3·2	$> 10^{8}$[e]
(6)	$Fe(phen)_3^{3+}$	$Fe(d\text{-}dipy)_3^{2+}$	+ 6	− 2·5	$> 10^{8}$[e]

[a] phen = 1,10-phenanthroline; d-dipy = 4,4′-dimethyl-2,2′-dipyridine; t-phen = 3,4,7,8-tetramethyl-1,10-phenanthroline; $Hb(H_2O)$ = ferrohæmoglobin.
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The relative slowness of the ferrohæmoglobin–ferricyanide reaction may be due to a type of steric hindrance in which the polypeptide chains prevent the close approach of the ferricyanide ions to the hæm-groups. In addition any hydrophobic groups on these polypeptide chains will tend to lower the dielectric constant in the vicinity of the hæm groups[10]. This will tend to increase the free energy of activation of the ferrohæmoglobin–ferricyanide reaction by the amount of work required to bring the ferricyanide ion from an environment of higher to one of lower dielectric constant[11]. In this connexion it is important to remember that electron transfer from the hæm group to the ferricyanide ion need not occur directly, but may occur via the polypeptide chains instead.

Another possibility is that the slowness of the ferrohæmoglobin–ferricyanide reaction is due to differences in the structures and solvations of ferro- and ferrihæmoglobin. It is apparent from reactions (1) and (2) of Table 1 that the replacement of cyanide ions in the co-ordination shells of the iron ions by water molecules leads to a marked decrease in the rate of the electron transfer reaction. Such decrease is generally ascribed to the differences in the structures of the inner hydration shells of the ferrous and ferric ions and the energy required to rearrange these shells before electron transfer can occur[11]. In a similar manner, any differences in the iron–oxygen and iron–nitrogen distances in the two oxidation states as well as any differences in the configuration of the surrounding solvent molecules will tend to slow down the rate of oxidation of ferrohæmoglobin. Because of the rigidity of the porphyrin rings, such effects are more likely to be associated with differences in the binding of the imidazole groups and the water molecules co-ordinated to the iron atoms in ferro- and ferrihæmoglobin.

It is interesting to recall that in addition to being relatively resistant to oxidation to the iron(III) state, the iron(II) in ferrohæmoglobin is able to co-ordinate oxygen rapidly and reversibly. This latter property requires that at least one of the ligands attached to the iron(II) be readily replaceable by oxygen[12]. In the case of ferrohæmoglobin this function is fulfilled by the water molecule attached to the iron(II). It is thus possible that this water molecule serves the dual purpose of enabling the ferrohæmoglobin to co-ordinate oxygen molecules rapidly and reversibly, and at the same time renders it relatively resistant to attack by such oxidizing agents as ferricyanide ions.

I wish to thank Dr. Gerald M. Edelman of the Rockefeller Institute, New York, for preparing the oxyhæmoglobin samples. This work was carried out under the auspices of the U.S. Atomic Energy Commission.

NORMAN SUTIN

Chemistry Department,
Brookhaven National Laboratory,
Upton, Long Island, New York.

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Structure and Spectra of $[(Phenanthroline)_2Fe(CNMe)_2]^{2+}$ and $[(Phenanthroline)_2Fe(CN)_2H^+]^{2+}$

THE striking shift in the position of the visible absorption bands of dicyano *bis*(1 : 10 phenanthroline) iron(II) and the corresponding 2-2′-dipyridyl complex caused by the addition of acid was first noted by Schilt[1], who has since shown that these compounds react reversibly to give mono- and di-protonated ions[2]. Schilt suggested that the hydrogen is attached directly to the metal in the protonated species. A second possibility is that the protonated compounds are '*iso*cyanides'.

Treatment of the phenanthroline compound with excess methyl sulphate gave an orange water-soluble product which precipitated from aqueous solution as the perchlorate on addition of excess sodium perchlorate. Analysis showed it to be the perchlorate of the dimethyl derivative of the original complex. It evolved methyl *iso*cyanide on warming in neutral aqueous solution.

The visible absorption spectrum of this compound is strikingly similar to that of the diprotonated form of Schilt's compound in 10 *M* sulphuric acid (Fig. 1). These facts together with the observation that the spectrum of the methyl derivative is essentially unchanged in 10 *M* sulphuric acid suggest strongly that the diprotonated ion should be written as an *iso*cyanide $[(phenanthroline)_2Fe(C \equiv NH)_2]^{++}$ analogous to the methyl derivative $[(phenanthroline)_2 Fe(C \equiv N.CH_3)_2]^{++}$.

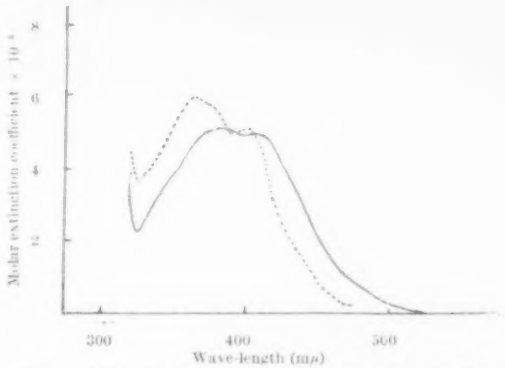

Fig. 1. Molar extinction curves for: (1) $[(phenanthroline)_2 Fe(CNMe)_2](ClO_4)_2$ in water (—); (2) $[(phenanthroline)_2 Fe(CN)_2]$ in 12 *M* sulphuric acid (Schilt) (. . . .)

In an attempt to decide whether the compounds have the *cis* or *trans* configurations we have measured their infra-red spectra in 'Nujol' mulls. In each case we find evidence of a splitting of the CN frequency into two peaks separated by about 10 cm.$^{-1}$ (Fig. 2). This suggests, but does not prove, that the compounds have the *cis* configuration.

The intense visible absorption band of the ferrous *tris*-phenanthroline complex has often been classified as a charge-transfer band associated with the photoreduction of the organic ligand by the metal ion[1]. Since there is no permanent reaction this interpretation cannot be confirmed directly by chemical methods. Our results lend strong support to the charge-transfer hypothesis.

We may safely assume that the intense visible absorption of $[Fe(phenan)_2(CN)_2]$ has the same origin as that of the *tris*-phenanthroline complex. When one CN^- ion is converted to a CNH group by protonation the absorption band moves from 6000 Å. to 5000 Å.

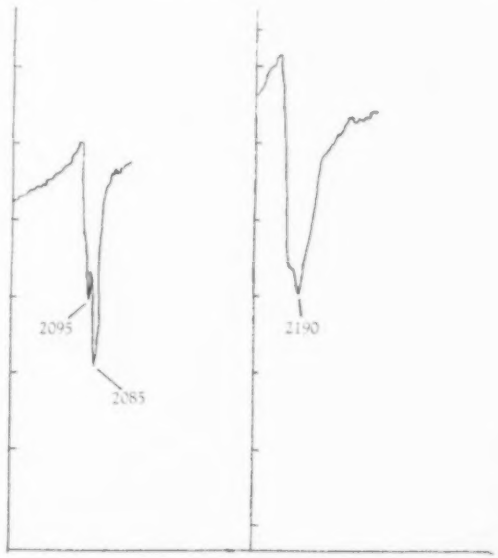

Fig. 2. Infra-red spectra of C ≡ N region: (1) $[(phenanthroline)_2 Fe(CNMe)_2](ClO_4)_2$; (2) $[(phenanthroline)_2Fe(CN)_2]$

When both CN⁻ groups are protonated or alkylated there is a shift of 3800 Å. We believe that the protonation (or alkylation) of the CN⁻ group transforms it from a moderate to a very strong π electron acceptor, for it is known that the *iso*nitriles resemble CO rather than CN⁻ in their ability to stabilize low valency states. The shift of the absorption spectrum is thus due to the stabilization of the ferrous state with respect to the ferric by the isonitrile group. The magnitude of the effect, about 0·6 eV. or 14 k.cal. per proton, is surprisingly large.

The visible band of the dicyanide is extremely sensitive to the nature of the solvent, moving to shorter wave-lengths as the solvent polarity is increased. This is understandable if we suppose that polar solvent molecules are strongly oriented in the neighbourhood of the cyanide groups by dipole-dipole interaction or by hydrogen bonding. Excitation leads to a quite new charge distribution in the complex which is no longer adjusted to the oriented solvent molecules. It follows that the greater the stabilization of the ion by solvent in the ground-state, the more the excitation energy is increased. Furthermore, since the nitrogen atoms of the cyanide groups lose negative charge during excitation any hydrogen bonds which they form will be weakened. These two factors account for the marked solvent effects.

N. K. Hamer
L. E. Orgel

Department of Theoretical Chemistry,
University Chemical Laboratory,
Lensfield Road, Cambridge.

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Interaction of Model Peptides with Water and Lithium Bromide

Knowledge of the interactions between peptide groups and water or denaturing agents is of major importance in understanding proteins. Klotz and Franzen[1] showed recently by infra-red studies that aqueous N-methylacetamide (NMA) forms few interpeptide hydrogen bonds except at concentrations approaching 12 *M*. Hydrogen bonds between water and NMA are formed more readily. Harrington and Schellman[2] proposed that the increased viscosity of proteins in strong lithium bromide solutions is the result of more extensive bonding and more helical coiling than in water, in contrast to the widely held

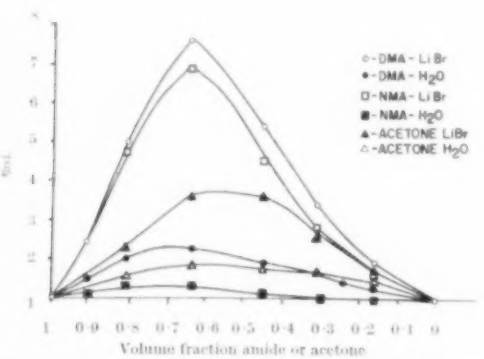

o-DMA - Li Br
•-DMA - H2O
□-NMA - Li Br
■-NMA - H2O
▲-ACETONE LiBr
△-ACETONE H2O
η rel
1·0 0·9 0·8 0·7 0·6 0·5 0·4 0·3 0·2 0·1 0
Volume fraction amide or acetone

Fig. 1. Viscosities of NMA, DMA and acetone in water and lithium bromide. Solutes were mixed with water or with 10 *M* lithium bromide to obtain the volume fractions indicated

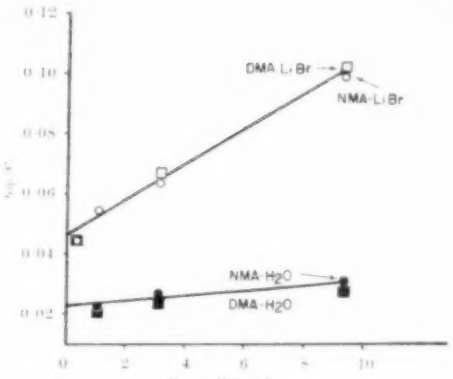


Fig. 2. Intrinsic viscosities of NMA and DMA in water and 9 *M* lithium bromide

idea that hydrogen bonds are broken in lithium bromide solution. We present viscometric data relating to the interaction of water solutions of lithium bromide with NMA, dimethylacetamide (DMA), acetone, and polysarcosine. The results show that increased viscosities occur in systems where interpeptide hydrogen bonds cannot form.

Fig. 1 shows that mixtures of NMA, DMA or acetone with water have viscosities higher than those calculated on the assumption of ideal mixing. Mixtures of NMA, DMA or acetone with 10 *M* lithium bromide have still higher viscosities, similar to those reported for the system urea–lithium bromide[3]. The maxima of the lithium bromide curves for DMA, NMA and acetone all occur at a ratio of solute to lithium bromide of nearly 2 : 1. 10 *M* potassium thiocyanate and 9 *M* guanidinium chloride raise the viscosity of acetone or NMA one-third to one-half as much as does lithium bromide.

Fig. 2 shows that the intrinsic viscosities of NMA and DMA are higher in lithium bromide solution than in water. (All the viscosities reported here were measured in Cannon Instrument Co. dilution Ubbelohde viscometers, sizes 50 or 75, at 39° C. The flow time for NMA in the semi-micro, size 50 viscometer was 13 min. and in size 75 was 8 min. for about 1 ml. of liquid.)

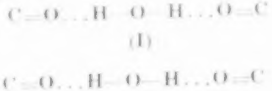
In Table 1 are shown viscosities of NMA and DMA in aqueous lithium halides, hydrochloric acid, and carbon tetrachloride. Lithium chloride and bromide give similar results, so that the effect must be largely due to the lithium ion. The similarity between NMA and DMA in Figs. 1 and 2 and Table 1 show that interpeptide hydrogen bonding need not be involved in lithium bromide solutions. In carbon tetrachloride the interpeptide hydrogen bond of NMA is apparent in the elevation of viscosity.

Table 1. Relative Viscosities of Amides in Several Solvents

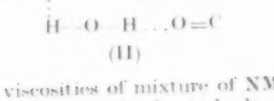
Volume and amide (ml.)	Volume and solvent (ml.)	Relative viscosity
10 NMA	1 10 *M* LiBr	2·14*
10 DMA	1 10 *M* LiBr	1·85*
10 NMA	1 10 *M* LiCl	2·32*
10 DMA	1 10 *M* LiCl	1·79*
10 NMA	1 10 *M* HCl	1·59*
10 DMA	1 10 *M* HCl	1·36*
1 NMA	9 10 *M* HCl	1·35†
1 DMA	9 10 *M* HCl	1·34†
1 NMA	9 CCl_4	1·66‡
1 DMA	9 CCl_4	1·06‡

* Relative to 10 ml. amide plus 1 ml. water.
† Relative to 9 ml. solvent plus 1 ml. water.
‡ Relative to pure carbon tetrachloride.

Of greater importance in relation to proteins is that the intrinsic viscosity of polysarcosine of molecular weight 2,500 (Schwartz Bio-Research, Inc., New York) was 0·086 in 9 *M* lithium bromide and 0·054 in *M* potassium chloride. These results for polysarcosine are contrary to those reported by Steinberg *et al.*[4] for poly-L-proline, which also cannot form interpeptide hydrogen bonds. Polysarcosine of higher molecular weight and copolymers of sarcosine and proline are being prepared for study, as are other copolymers.

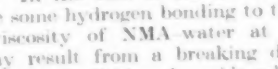


(I)

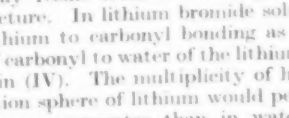


(II)

The high viscosities of mixture of NMA, DMA or acetone with water may be due to hydrogen bonding, as in (I) or as in (II). Two hydrogen bonds to one peptide carbonyl have been shown to exist in crystalline acetamide[5]. In the case of NMA and DMA there may also be some hydrogen bonding to the nitrogen. The low viscosity of NMA–water at high water content may result from a breaking down of the water structure. In lithium bromide solutions there may be lithium to carbonyl bonding as in (III), or bonding of carbonyl to water of the lithium hydration sphere as in (IV). The multiplicity of hydrogens in the hydration sphere of lithium would permit formation of larger aggregates than in water. At low peptide concentrations, multiple binding as in (III) or (IV) becomes less probable, and there may be only one peptide group bound for each lithium. The nature of the lithium to peptide bonding is not specified but may be similar to the ion-dipole attraction of lithium to water.



(III)



(IV)

Experiments were also done with 8 and 12·5 *M* lithium bromide acting on NMA. The maxima of the viscosity curves were 4·5 and 22 and occurred at ratios of amide to lithium of 3 : 1 and 1 : 1, respectively. 8, 10 and 12·5 *M* lithium bromide have water to lithium ratios of about 5, 3·7 and 3 respectively. It appears that lower hydration of lithium results in greater interaction with amides. This supports formulation (III) rather than (IV). However, lower hydrates would be expected to produce stronger hydrogen bonding as the strengthening effect of the lithium charge on the hydrogen bond would be distributed among fewer hydrogens. With 12 *M* lithium bromide the curve was not continuous, a crystalline precipitate appearing at an NMA volume fraction of 0·8. Determination of the structure of this precipitate by X-ray diffraction is planned.

In 10 *M* hydrochloric acid aggregation may be mediated by hydrogen bonding of H_3O^+ or $H_3O(H_2O)_n^+$ units to the carbonyl groups. Steinberg *et al.*[4] proposed protonation of peptide groups to explain the high optical rotation of poly-L-proline in strong acid.

The increased viscosity of proteins in strong lithium bromide solution may be due to extension of the polypeptide chain as a result of attaching many hydrated lithium ions in close proximity. The possibility of aggregation is also being investigated. In the case of poly-L-proline special configurational effects may be involved.

We are grateful to Dr. David Harker for suggesting hydrogen bonding of the lithium hydration sphere. This work was supported partly by a grant from the National Institutes of Health.

J. Bello
H. R. Bello

Department of Biophysics,
Roswell Park Memorial Institute,
Buffalo 3, New York.

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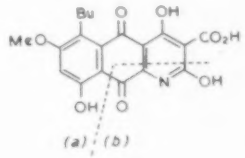
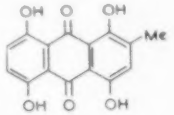
Pigments of *Phoma terrestris* Hansen and their Biosynthesis

Wright and Schofield[1] recently reported the failure of cultures of *Phoma terrestris* Hansen (from the Centralbureau voor Schimmelcultures, Baarn) to produce the pigment phomazarin[2] for which (I) is one of the two suggested structures. In our hands cultures from the same source have given this compound, which agrees well in physical properties with those described by Kögl *et al.*[2]. For reasons which we are unable to define, the same organism grown under the usual conditions[2] does not invariably produce the pigment. Like Wright and Schofield[1] we have observed cyanodontin (II) as a constituent of the mycelium.



(I)



(II)

Radioactivity from $^{14}MeCO_2Na$ and $Me^{14}CO_2Na$ is incorporated into cyanodontin. The acetic acid, obtained by Kuhn–Roth oxidation of the $^{14}MeCO_2Na$-derived material, had one-eighth of the total activity, all on the methyl group. The acetic acid obtained similarly from the $Me^{14}CO_2Na$-derived material had one-seventh of the total activity, all on the carboxyl group. This shows that cyanodontin in common with other natural 2-methylanthraquinones (for example, ref. 3) is biosynthesized through head-to-tail linkage of eight acetic acid units and loss of the carboxyl carbon from the end of the chain.

Radioactivity from $H^{14}CO_2Na$, $^{14}MeCO_2Na$ and $Me^{14}CO_2Na$ is incorporated into phomazarin. Degradation has shown that about 75 per cent of the activity of the $H^{14}CO_2Na$-derived material is located on the methoxyl carbon, the remainder being ran-

doubly distributed over the carbon skeleton. Therefore the latter is formed probably without the intervention of C_1-units (cf. ref. 4). The acetic acid obtained by Kuhn–Roth oxidation and the carbon dioxide formed by decarboxylation of the $^{14}MeCO_2Na$-derived material each had approximately one-eighth of the total activity. The acetic acid obtained by Kuhn–Roth oxidation of the $Me^{14}CO_2Na$-derived material had approximately one-eighth (12·1 per cent) of the total activity, 98 per cent of it on the carboxyl group. This suggests that the biosynthesis of phomazarin involves at least eight acetic acid units and implies that the nitrogen-containing moiety may be derived from an amino-acid (cf. terramycin[3]), possibly glycine. The derivation of the carboxyl carbon from the methyl carbon of acetic acid favours a structure of type (I) over an alternative which has the terminal benzene ring inverted. If structure (I) is correct then the dotted line dissects the skeleton into portions which could be derived from (*a*) eight acetic acid units linked head-to-tail, and (*b*) glycine. Further degradations are in progress.

A. J. Birch
R. I. Fryer
P. J. Thomson
Herchel Smith

Department of Chemistry,
The University,
Manchester, 13.

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BIOCHEMISTRY

Amino-acid Synthesis from Hydrogen Cyanide under Possible Primitive Earth Conditions

The formation of adenine from hydrogen cyanide has been recently reported from this laboratory[1]. Continuing the work on the synthesis of biochemical compounds under possible primitive Earth conditions[2], we now have investigated the direct formation of amino-acids from hydrogen cyanide.

Gaseous hydrogen cyanide was slowly introduced into 1 litre of 3 *N* ammonium hydroxide placed in a 2-litre flask provided with a water-cooled condenser. At the end of 1 hr., the flow of gas was stopped and the reaction mixture was analysed for cyanide ion by the method of Schilt[3]. It was found 2·2 *M* in this ion.

The alkaline aqueous solution was heated at 70 ± 2° for 25 days, after which time the black polymer of hydrogen cyanide[4] was removed by centrifugation. The reddish supernatant solution was fractionated by ion exchange into two main fractions and the fraction containing the amino-acids was analysed by one- and two-dimensional paper chromatography.

For the ion exchange fractionation, 200 ml. of the supernatant were added to the top of a 4 × 40 cm. column of 'Dowex 2' resin (200–400 mesh, *X* 8, OH form). The column was first washed with water until the effluent was neutral and then the acidic and ampholytic components bound to the resin were eluted by means of 4 *N* acetic acid. A total volume of 1,200 ml. was collected in three sub-fractions of 400 ml. each. The first of these sub-fractions was essentially neutral and corresponded to the water hold-up volume of the column, which emerged just before the acetic acid solvent front. The second and third sub-fractions were, as expected, strongly acidic.

A preliminary paper chromatographic analysis indicated that almost all the amino-acids were present in the second sub-fraction. This solution was concentrated to dryness in a vacuum-rotating evaporator at 60°, then dissolved in 25 ml. of 1 *N* hydrochloric acid and analysed by paper chromatography.

For this, 25 µl. of the red-yellowish solution was placed on a small sheet of Whatman No. 3 mm. filter paper and chromatographed by ascending development, first in *n*-butanol/acetic acid/water, 4 : 1 : 1, and then, on drying, in *n*-propanol/1 *N* ammonium hydroxide, 3 : 1. The paper was then sprayed with 0·2 per cent ninhydrin in *n*-butanol and heated in the oven for 5 min.

Fig. 1 shows, on the right side, a two-dimensional chromatogram of the unknown; on the left side, a one-dimensional chromatogram of the standards glycine and alanine, of the unknown, and of a mixture of standards and unknown.

On the basis of this and other chromatographic evidence, the amino-acids alanine, glycine and aspartic acid, which correspond to the top three spots of the two-dimensional chromatogram, were tentatively identified among the products formed by the condensation of hydrogen cyanide in aqueous ammonia. The other spots have not yet been identified. The compound close to the origin, slowly migrating, developed maximum colour intensity only after a few days, indicating that it may be a peptide(s) or a compound of a similar behaviour to a peptide. Total amino-acids were quantitatively determined by the method of Troll and Cannan[5], and found to amount to 10 m*M*/l. of original reaction

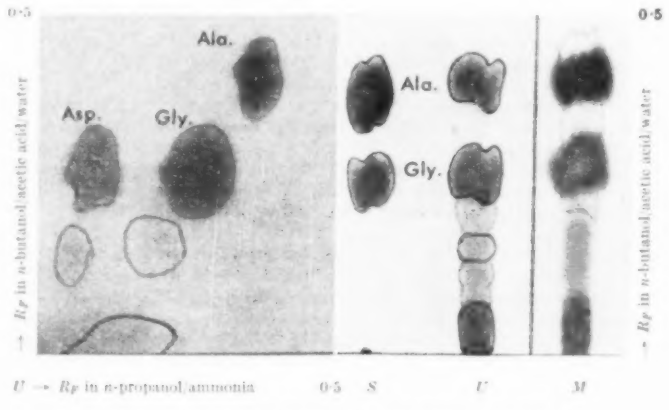

Fig. 1. Photographs of two chromatograms of the hydrogen cyanide reaction product after its elution from a 'Dowex 2' column by acid. *S*, Standards, alanine and glycine; *U*, unknown; *M*, mixture of standards and unknown

mixture, measured as glycine. This represents a substantial yield if it is considered that most of the hydrogen cyanide is condensed into polymeric hydrogen cyanide[4].

When 100 µl. aliquots of the test solution were chromatographed, small spots of several other ninhydrin-positive compounds were observed. In addition, by means of a Mineralight lamp (2537 A.) a number of ultra-violet-light absorbing and fluorescent spots were detected on two-dimensional chromatograms.

In line with the above results, Wippermann[6] and other workers[4] demonstrated many years ago the formation of glycine by mild alkaline hydrolysis of an oligomer of hydrogen cyanide which had been obtained from hydrogen cyanide by base catalysis. It is possible that the well-established tetramer of hydrogen cyanide, di-aminomaleonitrile[7], and its assumed intermediate, aminomalonitrile[8], are the precursors of the C_2-, C_3- and C_4-amino-acids obtained in the present experiments.

Work is in progress for the identification of all the amino-acids, for the elucidation of the mechanism of amino-acid synthesis, and for determination of the nature of the other compounds synthesized from hydrogen cyanide.

This work has been supported in part by research grant No. G-13117 from the National Science Foundation and will be reported in more detail elsewhere.

J. Oró
S. S. Kamat

Chemistry Department,
University of Houston,
Houston 4,
Texas.

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Occurrence of *n*-Odd-Numbered Monoethylenic Fatty Acids in the Liver Oil of the New Zealand School Shark (*Galeorhinus australis* MacLeay)

Investigations on the minor fatty acid constituents of the liver oil of the New Zealand school shark have resulted in the isolation of the saturated *n*-odd-numbered acids as well as the *iso*- and (+)-*anteiso* acids of the C_{15} and C_{17} series[1,2]. These acids had not previously been found in fish oils, but had been earlier isolated from the depot[3] and milk fats[4] of ruminants. In addition, the occurrence of *n*-heptadecanoic acid and of (+)-14-methylhexadecanoic acid in tall oil has been established[5]. The occurrence of *n*-odd-numbered unsaturated acids in animal depot fats was first recorded in lamb caul fat, from which Δ^9-heptadecenoic acid was isolated[6] and the presence of pentadecenoic acid indicated: Δ^9-heptadecenoic acid has also been obtained from musk-ox fat[7] and from butterfat[8]. Following the feeding of *n*-odd-numbered saturated fatty acids, Appel, Böhm, Keil and Schiller[9] found that the corresponding Δ^9-mono-unsaturated acids were deposited in the depot and milk fats of goats and sheep. Apart from the above-mentioned instances, however, *n*-odd-numbered unsaturated acids have not been isolated from depot fats.

In shark liver oil, following extensive ester fractionation and low-temperature crystallization, fractions containing concentrates of *n*-mono-unsaturated acids of the C_{15}, C_{17} and C_{19} series have been prepared. These fractions have now made possible the isolation of Δ^9-heptadecenoic acid in pure form, and of Δ^{11}-nonadecenoic acid as a concentrate (73 per cent) with positional isomers mainly Δ^{10-} (13 per cent) and Δ^{12-} (14 per cent) nonadecenoic acids as impurities as judged from the yields of dibasic acids produced by oxidation using the method of Haverkamp Begemann *et al.*[10]. The resolution of these positional isomers is likely to prove difficult in contrast to the Δ^9-heptadecenoic acid, which was relatively easy to crystallize in pure form. From the weights of the concentrates and the results of gas-liquid chromatographic analysis it is estimated that pentadecenoic acid, Δ^9-heptadecenoic acid and Δ^{11}-nonadecenoic acid respectively form 0·018, 0·073 and 0·042 per cent of the shark liver oil fatty acids. These results serve to extend the similarities of ruminant fats and shark liver oils in regard to the occurrence of *n*-odd-numbered saturated and unsaturated fatty acids in addition to *iso*- and (+)-*anteiso*-acids of the C_{15} and C_{17} series earlier reported. Work on the isolation of the *n*-odd-numbered mono-unsaturated fatty acids is being continued.

Isobel M. Morice
F. B. Shorland

Department of Scientific and Industrial Research
Fats Research Laboratory,
Wellington,
New Zealand.

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Scorpamins : the Toxic Proteins of Scorpion Venoms

Following preliminary work[1,2], extensive purification of the toxins secreted by two species of North-African scorpions (*Androctonus australis* and *Buthus occitanus*) was accomplished by aqueous extraction, acetone fractionation in the cold, chromatography on 'Amberlite *CG* 50' and filtration on dextran gel ('Sephadex *G* 25'). Table 1 summarizes the steps of purification from the glands.

Comparative experiments were performed, starting with the organ containing the venom glands (telson) or with the emitted venom obtained by a manual or an electrical method previously described[1]. The

Table 1. Purification of Scorpamins starting with the Telsons of *A. australis* and *B. occitanus*

Steps of purification	*Androctonus australis* (15·29 gm. lyophilized telsons)				*Buthus occitanus* (4·75 gm. lyophilized telsons)			
	A_{280} *	LD_{50}†	*SA* ‡	Yield (per cent)	A_{280}	LD_{50}	*SA*	Yield (per cent)
Extraction by NaCl 0·9 (per cent)	3,180	33,333	10·5	100	4,768	12,308	2·5	100
Acetone fractionation (60–80 per cent)	199	12,545	63	37·6	288	8,182	28·4	66·8
Chromatography on 'Amberlite *CG* 50' ammonium acetate, 0·5 *M*, *p*H = 5·60 §	18·9	4,723	250	14·2	347	2,313	72	18·8
Filtration on 'Sephadex *G* 25' ‖	—	—	—	—	15·7	1,577	100	12·8
Chromatography on 'Amberlite *CG* 50' ammonium acetate, 0·2 *M*, *p*H = 6·80¶	—	—	—	—	0·64	123	192	1

* Absorbance at 280 mμ.
† Number of lethal doses, 50 per cent, determined in a 20-gm. mouse according to Behrens and Karber (ref. 3).
‡ Specific activity = LD_{50}/A_{280}.
§ Dimensions of the column 4 cm. × 110 cm.
‖ With water as eluant. In this condition the toxin is adsorbed and can be eluted with ammonium acetate 0·05 *M*.
¶ Dimensions of the column 4 cm. × 135 cm.

Table 2. Purification of Scorpamins from *A. australis* starting with Electrically or Manually obtained Venom

Steps of purification	Venom extracted by the electrical method (105·9 mgm.)				Venom extracted by the manual method (114·5 mgm.)			
	A_{280}	LD_{50}	*SA*	Yield (per cent)	A_{280}	LD_{50}	*SA*	Yield (per cent)
Aqueous extraction	92	6,157	66·5	100	89·1	25,396	284·9	100
Filtration on 'Sephadex *G* 25'	34·2	4,046	118·3	65·7	48·7	20,160	413·8	79·4
Chromatography on 'Amberlite *CG* 50' ammonium acetate 0·2 *M*, *p*H = 6·80 *	3·4	1,870	550 †	30·4	14·3	7,961	556 †	31·3

See Table 1 for explanations of abbreviations.
* Column dimension, 4 cm. × 145 cm.
† One LD_{50} corresponds to 1·0 μgm. of pure toxin.

purification procedure is less tedious starting with the desiccated venom according to its higher toxin content (Table 2). The yield in pure toxin is about 30 per cent in these conditions.

The material obtained after the last step on 'Amberlite *CG* 50' was homogeneous with regard to chromatography (constant specific activity) (Fig. 1), electrophoresis and in the ultracentrifuge.

Two proteins, sharing almost equally the total toxic activity, have been separated from the venom of both species (Fig. 1). Their properties are very similar considering specific activity (the two toxins of *A. australis* and one of the two toxins of *B. occitanus* have specific activity of about 500), molar extinction coefficient and symptomatology of the intoxication in mice.

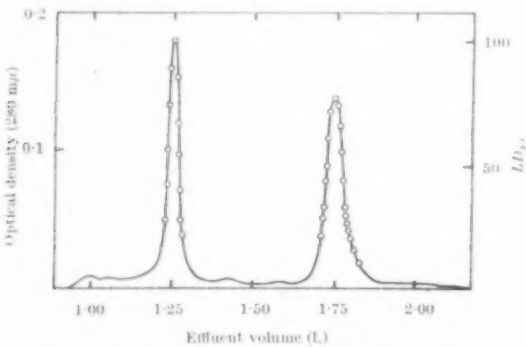

Fig. 1. Chromatographic homogeneity test of the pure toxins of *A. australis* on 'Amberlite *CG* 50' (4 cm. × 145 cm. column) equilibrated with ammonium acetate 0·2 *M*, *p*H = 6·80. Venom obtained by the manual method after filtration on 'Sephadex *G* 25'. The curve in full line corresponds to the optical density at 280 mμ. Open circles express the toxic activity in LD_{50} for the 20-gm. mouse, tested in several tubes of the separated peaks

Preliminary investigations indicate a molecular weight of 12,000 for the toxic proteins of *B. occitanus*, and a *p*H_i around 8·5 for the toxins of both species. The generic name of scorpamins has been given to the toxins of scorpions[2].

The venom collected by the manual technique is better for obtaining the pure toxins with a good yield (Table 2). The main characteristics of scorpamins are: (1) their pure neurotoxic effect; (2) their low molecular weight; (3) their high resistance to storage and denaturating agents. With regard to these properties, scorpamins constitute a remarkable material for the study of mechanism of action of neurotoxic proteins.

Full details of these experiments will be published elsewhere.

Francois Miranda
Serge Lissitzky

Laboratoire de Chimie Biologique,
Faculté de Médecine et de Pharmacie,
Marseille.

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Reaction of Antimony Pentachloride with Pregnane-3α, 17α, 20α-Triol, Pregnane-3α, 17α, 20α-Triol-11-One and Other Adrenal Cortical Steroids

Antimony pentachloride has been used for detecting a number of steroids on paper chromatograms[1–4]. Pregnane-3α, 17α, 20α-triol (pregnane-triol) and pregnane-3α, 17α, 20α-triol-11-one (preg-

pregnanetriolone) can be detected on paper chromatograms by the method of Finkelstein and Cox[2] in which 70 per cent phosphoric acid induces a pink fluorescence in the former and a brilliant blue fluorescence in the latter when viewed with a long-wave (3660 Å.) ultra-violet lamp. However, the phosphoric acid gradually destroys the chromatogram paper, which necessitates delicate manipulation to avoid shredding.

We have found that antimony pentachloride can be used as a detecting agent for both pregnanetriol and pregnanetriolone.

Pregnanetriol (obtained from Mann Research Laboratories, Inc., New York, N.Y., and Sigma Chemical Co., St. Louis, Missouri); pregnanetriolone (obtained from Dr. W. Klyne, Steroid Reference Collection, Postgraduate Medical School, London, and Dr. M. Finkelstein, Hormone Research Laboratory, Hadassah Medical School, Jerusalem); pregnane-3α, 11β, 17α, 20α-tetrol (pregnanetetrol), and pregnane-3α, 17α, 20β-triol-11-one (pregnanetriol β-epimer) (obtained from Dr. D. Fukushima, Sloan Kettering Institute, New York, N.Y.) were placed on Whatman No. 1 paper in 50-μgm. amounts and sprayed with 20 per cent antimony pentachloride in chloroform (20 gm. in 100 ml.). Immediately the pregnanetriol and pregnanetetrol turned yellow in colour. The pregnanetriol darkened and turned dark brown, while the pregnanetetrol changed to a bright blue colour. Pregnanetriolone in 50-μgm. amounts gave a yellow colour. With less than 50-μgm. amounts the pregnanetriolone and the pregnanetriolone β-epimer gave no visible reaction.

The paper was then heated for 5 min. at 78° C. The pregnanetriol became blue-grey in colour, and the pregnanetetrol became brown-grey. The pregnanetriolone became yellow in colour, while the pregnanetriolone β-epimer became faint yellow. Table 1 summarizes the results. Before heating only 50 μgm. of pregnanetriolone could be detected, while at least 5 μgm. of pregnanetriol gave a colour reaction. After heating, 5 μgm. of pregnanetriolone was faintly visible.

Table 1. Reaction of Adrenal Cortical Steroids with Antimony Pentachloride

Compound	Colour before heating	Colour after heating
Pregnane-3α, 17α, 20α-triol	Yellow → dark brown	Blue-grey
Pregnane-3α, 11β, 17α, 20α-tetrol	Yellow → blue	Brown-grey
Pregnane-3α, 17α, 20α-triol-11-one	No colour	Yellow
Pregnane-3α, 17α, 20β-triol-11-one	No colour	Faint yellow
Hydrocortisone	No colour	Pale yellow
Cortisone	No colour	Very faint yellow
Corticosterone	No colour	Yellow
11-Deoxy-17 hydroxycorticosterone	No colour	Grey
11-Dehydrocorticosterone	No colour	Very faint yellow
11-Deoxycorticosterone	No colour	Blue

Other steroids including hydrocortisone, cortisone corticosterone, 11-deoxy-17 hydroxycorticosterone, and 11-dehydrocorticosterone gave no colour reaction with antimony pentachloride before heating. However, after heating for 5 min. at 84° C. corticosterone gave a yellow colour, 11-deoxycorticosterone a blue colour, 11-deoxy-17-hydroxycorticosterone a grey colour, and hydrocortisone a pale yellow. Cortisone and 11-dehydrocorticosterone gave very faint yellow colours which might not be detected if one did not know exactly where the compounds were located. These results are shown in Table 1.

These reactions with antimony pentachloride have been very useful in locating these various steroids on paper chromatograms because of the simplicity of the method.

Robert H. Herman
Joseph Bruton

Department of Metabolism,
Division of Medicine,
Walter Reed Army Institute of Research,
Walter Reed Army Medical Center,
Washington, D.C.

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Action Pattern of β-Amylase

Current opinion with respect to the action pattern of β-amylase on amylose is divided into three divergent points of view: (1) single-chain pattern, in which β-amylase, having commenced attack on a given amylose molecule, completely hydrolyses this molecule to maltose before attacking another molecule; (2) multi-chain pattern, in which β-amylase removes a single maltose molecule from the non-reducing terminus of an amylose molecule, then completely separates from the substrate molecule and continues the attack on other amylose molecules in the same way; (3) multiple attack, in which β-amylase remains associated with a given amylose molecule long enough to remove, on the average, several molecules of maltose before attacking another amylose molecule. Substantial evidence exists which can be interpreted in favour of each of these points of view[1–5].

The principal evidence for the single-chain pattern is that at intermediate stages during action of β-amylase on amylose, the residual amylose remains essentially unchanged with respect to such properties as molecular weight, viscosity, and iodine colour[1–4]. With multi-chain or multiple attack it would be expected that the molecular weight of the remaining amylose would gradually decrease during β-amylase action. A critical feature of this interpretation, which has not been adequately considered, is the nature of the chain-length distribution of the original amylose as well as that of the amylose remaining at intermediate stages of hydrolysis. Specifically, if the molecular weight distribution of the original amylose is the 'most probable' distribution[2], any of the three

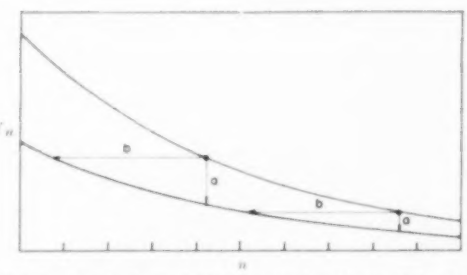

Fig. 1. Attack of 'most probable' amylose by (*a*) single-chain, (*b*) multi-chain action patterns. In (*a*) the number X_n of chains of a given length n is reduced by a given proportion. In (*b*) each chain is shortened by a given amount. The two action patterns are seen to give rise to identical distributions at intermediate stages of degradation. X_n and n are on an arbitrary scale

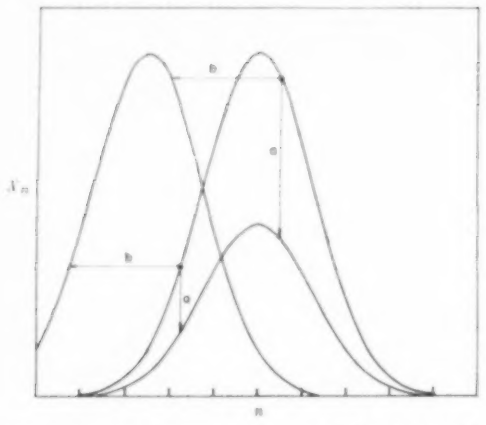

Fig. 2. Attack of 'normal distribution' amylose by (*a*) single-chain, (*b*) multi-chain action patterns. With (*a*) the distribution is unchanged but with (*b*) the average molecular weight is much reduced

suggested action patterns will lead to average molecular weights and size distributions of the residual amylose precisely the same as those of the original amylose. On the other hand, if the distribution of the original amylose is of the Gaussian or Kraemer-Lansing type, multiple attack or multi-chain action patterns would lead to products of substantially lower average molecular weight. These statements, illustrated qualitatively in Figs. 1 and 2, have been proved by exact mathematical analysis. For multiple attack the results are similar to those with the multi-chain pattern.

Most recent evidence is that native amylose corresponds to the 'most probable' distribution[5]. Moreover, while random degradation during preparation of amylose will reduce its average molecular weight, it is expected that the degraded material will still correspond to the 'most probable' distribution[7]. Hence, with native or unfractionated degraded amylose, one cannot distinguish between single-chain, multi-chain, and multiple-attack action patterns.

On the other hand, by synthesis or fractionation, it should be possible to produce high-molecular-weight amylose preparations with molecular size distributions significantly different from the 'most probable' distribution[8], and such materials are the only suitable substrates for definitive studies of the action pattern of β-amylase on high-molecular-weight amylose.

Dexter French

Department of Biochemistry and Biophysics,
Iowa State University,
Ames,
Iowa.

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A Difference between the Modes of Action of Substrate and Hormonal Inducers of Rat Liver Tryptophan Pyrrolase

The level of tryptophan pyrrolase can be greatly increased in rat liver by the intraperitoneal injection of tryptophan[1], cortisone[2] or hydrocortisone[3]. The administration of adrenocortical hormones is not associated with an increased level of tryptophan in the liver[3]. Moreover, cortisone is a non-specific inducer, in that it affects the levels of several liver enzyme systems[3]. Reserpine[4] has also been shown to increase the level of activity of tryptophan pyrrolase, and since it does not elicit this response in hypophysectomized rats, it has been suggested that its effect is mediated by the pituitary–adrenal system[3]. The present work indicates a qualitative difference in the mode of action of tryptophan on one hand and cortisone and reserpine on the other in the induction of tryptophan pyrrolase.

It has been shown previously[6,7] that rat liver tryptophan pyrrolase is located in the particle-free cell sap and that microsomes, owing to their iron-protoporphyrin content, can activate the enzyme of normal rat liver to a value approximately three times that of unsupplemented cell sap. It can be seen from Fig. 1 that the addition of liver microsomes, from either cortisone-treated or normal rats, causes similar relative increases in the tryptophan pyrrolase activity of liver cell sap preparations from both normal and cortisone-treated rats. Thus, following cortisone treatment, the rise in enzyme-level is not accompanied by a significant increase in the relative amount of available activator. Similar results were obtained when using reserpine as the inducing agent. Table 1 summarizes these results and contrasts them with those obtained following treatment with tryptophan. It can be seen that whereas the ratio of unstimulated to fully stimulated cell sap tryptophan pyrrolase activity has not been changed significantly by treatment with cortisone or reserpine, it has been greatly increased by tryptophan treatment. Although the maximal activity obtainable, presumably reflecting the amount of tryptophan pyrrolase apoprotein, was the same following administration of either tryptophan or cortisone, the effective enzyme activity (in

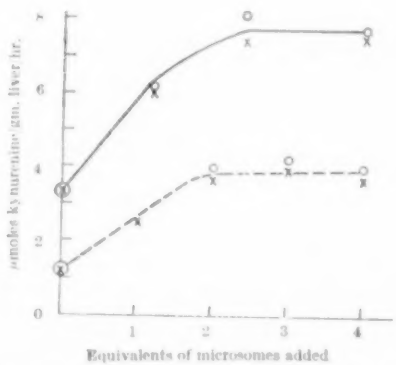

Fig. 1. Effect of microsomes on liver cell sap tryptophan pyrrolase activity of normal and cortisone-treated rats. Liver microsomes and particulate-free cell sap were obtained from normal rats and from rats killed 2 hr. after intraperitoneal administration of cortisone (10 mgm./kgm.). Normal cell sap (– – –); cortisone-cell sap (——); normal microsomes (×); cortisone-microsomes (○). The addition of one equivalent of microsomes restores the microsome–cell sap ratio to that of unfractionated liver homogenate

Table 1. Induction of Tryptophan Pyrrolase by Different Agents

Cortisone ('Cortisoneacetate', Merck) (0·01 gm./kgm.) and L-tryptophan (1 gm./kgm.) were injected intraperitoneally, and reserpine ('Serpasil', Ciba) (0·001 gm./kgm.) subcutaneously. The four equivalents of microsomes employed gave maximal stimulation

Substance injected	Hours post-injection	Tryptophan pyrrolase activity (μmoles kynurenine/gm. liver/hr.) Unsupplemented cell sap	Cell sap + four equivalent microsomes
—	—	1·6	5·9
Tryptophan	1	2·8	6·0
	2	8·4	8·8
	4	13·0	15·8
Cortisone	1	2·0	5·2
	2	2·8	8·0
	4	4·8	16·0
Reserpine	2	2·6	4·4
	4	3·6	7·8

the absence of added activator) was much greater following treatment with tryptophan.

Previous work with tryptophan[7] suggested that the activation of tryptophan pyrrolase provides the stimulus for induction (defined as increase in total obtainable activity). In the case of cortisone and reserpine, such an activation does not take place, indicating an alternative mechanism for the initiation of enzyme induction.

This work was supported in part by the National Science Foundation (grant *NSFG* 11430) and the U.S. Public Health Service (grant CY 2332).

Olga Greengard
Philip Feigelson*

Departments of Biochemistry and Medicine,
College of Physicians and Surgeons,
Columbia University,
New York City.

* Investigator, Health Research Council, New York City, N.Y.

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Biosynthesis of Citrulline in Plants

In 1930 citrulline was discovered in water-melons[1]. Later it was shown to be an important participant in the Krebs and Henseleit ornithine cycle in animals and micro-organisms. In recent years several laboratories have worked on the ornithine cycle in plants. In this laboratory citrulline has been shown to play an important part in transporting and storing nitrogen in several families of higher plants[2–4]. Relatively high concentrations of citrulline in exuding sap and citrulline accumulated in artificially rooted leaves of alder trees show the root to have a determining influence in the biosynthesis of citrulline. However, excised branches of alder and hazel could also synthesize citrulline from ammonium nitrate under aseptic conditions. Though ornithine, the precursor of citrulline, is metabolized very quickly, we could not find significant amounts of it, but very high concentrations of the mono-N-acetyl-ornithine were found in all members of the family Fumariaceae, being characteristic of this family[5]. Ornithine reacting with carbamyl phosphate in the presence of carbamyl-transpherase is converted into citrulline. My experiments have shown this reaction to occur under physiological conditions even without enzyme, though converting carbamyl phosphate much more slowly to cyanate, which reacts with the amino-groups[6,7]. It was also possible to establish the biosynthesis of citrulline from ornithine and carbamyl phosphate in higher plants[8–11].

To examine the possibility of activity of carbamyl phosphate in seaweeds, different green, brown, and red algae were ground in a mortar with *tris* buffer *p*H 8 at + 4° C. The extract, being usually weakly acid, was brought up to *p*H 8 with sodium bicarbonate, centrifuged (30 min. at 7,000 r.p.m. at 5° C.), and incubated at 30° C. The reaction was stopped by freezing at −20° C., and the lyophilized reaction mixture re-solved with 70 per cent ethanol immediately before determination. After separation on paper chromatograms the amino-acids were determined colorimetrically with ninhydrin by comparison with standards[4].

The results given in Table 1 show that green and red seaweeds are able to synthesize citrulline from ornithine and carbamyl phosphate. 70–80 per cent of the ornithine was metabolized within the period of reaction. During this time some amino-acids increased also; primarily citrulline and glutamic as well as aspartic acid in small amounts, but not arginine and urea. After 30 min. incubation I found most of the initially produced ornithine was metabolized to citrulline; and there is scarcely a difference between incubation for 30 min. or 6 hr. Before incubation I found a relatively high concentration of citrulline in *Gracilaria*; whereas citrulline synthesis does not occur in *Taonia*. For the present we must leave it undecided whether this lack of citrulline synthesis is dependent on the developmental state of the plant, or whether it is specific only to *Taonia* or for all brown algae, having a special place in the biochemistry of seaweeds.

Table 1. Biosynthesis of Citrulline in Seaweeds

The complete system contained: 10 μmoles ornithine, 10 μmoles carbamyl phosphate (CP), 5 μmoles magnesium chloride, 1 ml. plant extract (= 1·5 gm. fresh weight of algae extracted and made up to 1 ml. with *tris* buffer *p*H 8)

	μMoles citrulline/1 ml. plant extract			
	Complete system	Complete system	Without CP	Without ornithine
Time of incubation (hr.)	0·5	6	6	6
Green algae				
Cladophora prolifera	6·85	8·60	0	0
Ulva lactuca	3·43	4·00	0·80	0
Red algae				
Neomonospora furcellata	6·29	6·85	1·60	0·69
Gracilaria conferoides	12·00	14·85	8·60	6·58

This work was carried out at the Stazione Zoologica, Napoli.

G. Reuter

Institut für Biochemie der Pflanzen,
Deutsche Akademie der Wissenschaften zu Berlin,
Halle.

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A New Preparation of Gastrin: Preliminary Characterization

This Laboratory is examining the chemistry of 'gastrin', about which little has been reported. We have recently prepared a gastrin-like secretory stimulant from porcine antral mucosa by a new and somewhat novel method. This is a preliminary report on its chemical properties, and similar data on 'gastrin' as prepared by a more conventional procedure. The quotation marks signify only that it is not known whether gastrin is a single compound, or a group of similar structures with a common unique moiety, or a group of biologically, more or less, specific substances. The facts that gastrin has been reported as dialysable[1], non-dialysable[2], with an isoelectric point near *p*H 5·0[3], or *p*H 8·0[4], to name only a few of its properties, leave the question very much open. Recently, Gregory *et al.*[5] described a gastrin-like substance isolated from a pancreatic tumour.

Different from any method we have found in the literature of this substance, we have extracted gastrin from hog antrum with aqueous alkali, *p*H 11–12, at 40° C. Subsequent steps included isoelectric precipitations at *p*H 5·0, and precipitations in sodium chloride solution. At no time was the preparation more acid than *p*H 4·0, or warmer than 40° C. Dialysis of the crude material against running water and several changes of distilled water followed by lyophilization or isoelectric precipitation gave yields of 0·5–2·0 gm. per 20 antral mucosæ.

At this stage we have had consistently good stimulation. Solutions of 75–100 mgm. (as little as 50 mgm. has produced good response) in 50 ml. of sterile saline were injected during ~30 min., using a motor-driven syringe. A sharp rise in secretory flow and of [H^+] resulted, followed by a decline after the injection. For the half-hour of greatest activity, eleven experiments gave us an average rate of secretion of 12·4 ml./hr., and a rate of hydrogen ion production equivalent to 18·0 ml. of 0·01 *N* hydrochloric acid/hr. 80 per cent, or more, of these amounts represented increase over the base line. Our best eight experiments with material prepared by a modification of the Uvnäs method[3] gave comparable figures of 5 ml. (volume) and 10·6 ml. (0·01 *N* hydrochloric acid equivalent.

In our previous work on dialysed gastrin, as prepared by the Uvnäs method, we had often noted vomiting, or an inactive preparation, or acquired tolerance. In the dialysed material from the new method we have not observed such symptoms, and we have had no inactive preparations. Of considerable additional interest are the excellent results obtained with subcutaneous injections. A good flow persisted for 2½–3 hr. after the injection, contrasting with the rapid decline after histamine injection. One such active sample had been kept dry and in the dark at −20° C. for 8 months before the assay.

In the material prepared by acid extraction and trichloracetic acid precipitation[3] we had found a small but consistent content of phosphorus (average 0·05 per cent). We have found 10–15 times as much phosphorus in the new preparation (dialysed), that is, 0·5–0·8 per cent. Treatment with 0·25 *N* alkali at 27° C., isoelectric precipitation and re-dialysis did not lower the phosphorus content appreciably, making the presence of a typical phosphoprotein unlikely[6].

In the ash of the dialysed gastrin, as the only unique constituent in measurable quantity, we have consistently found tin. On standing in dilute stannous chloride and prolonged re-dialysis, the gastrin retained considerable metal ion (ash ~1 per cent, of which ~20 per cent was tin).

We have subjected the dialysed gastrin to diethylaminoethylcellulose ion-exchange treatment, Tiselius electrophoresis (one main component, through the kindness of Dr. P. D. Goldsworthy), and curtain electrophoresis with veronal buffer (*p*H 8·6, ionic strength 0·02) on Whatman 3-*MM* paper at 300–500 volts. The most interesting results have come from the last method. Electrophoresis of a 1 gm. sample of dialysed material led to recovery of 65 per cent (redialysed and lyophilized material). One main protein fraction was observed (~40 per cent) which migrated (minus to plus) a moderate distance, and gave strong colour with tetrabromophenolphthalein ethyl ester (potassium salt)[7]. Displaced further toward the positive pole, there was a smaller fraction (average 2–3 per cent after dialysis), which gave no protein colour test, and another protein-like material (~1 per cent). The phosphorus content of the main protein fraction was low (0·05 per cent or less); that of the non-protein fraction was high (4–7 per cent). The main fraction had an ultra-violet spectrum typical for proteins. The ultra-violet spectrum of the non-protein fraction had a sharp intense peak at 260 mμ. Much of the remaining phosphorus, which had not been accounted for, appeared to be on the curtain in the path of the main protein fraction. The latter appears to be bound to the high-phosphorus fraction somewhat tenaciously.

The protein after electrophoresis had considerably less secretory stimulant activity than the material before electrophoresis and appeared to be less stable. The dialysed gastrin and the main protein fraction on electrophoresis have each given a 10 per cent yield, or more, of crystalline material, as long fibrous needles, by an ammonium sulphate procedure. Full details of the extraction procedure, the chemical properties and our experience in tracing the activity will be presented shortly.

This investigation was supported in part by Grant A-2341, from the National Institute of Arthritis and Metabolic Diseases, U.S. Public Health Service.

T. Lloyd Fletcher
Walter R. Anderson
Clifford L. Pitts
Richard L. Cohen
Henry N. Harkins

Chemistry Research Laboratory,
Department of Surgery,
University of Washington
School of Medicine,
Seattle 5.

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PHYSIOLOGY

Crystallization of Purines in the Vacuole of *Candida utilis*

We have reported previously that *Candida utilis* removes seven purines (adenine, guanine, hypoxanthine, xanthine, uric acid, 2,6-diaminopurine and *iso*guanine) from the medium by an active transport process when these compounds are used as sources of nitrogen for the yeast[1,2]. These compounds and their metabolic products are held within the cell in high concentrations that appear to exceed the solubilities of the compounds in the volume of water available. For example, 5 gm. (wet weight) of yeast that had taken up 4·50 mgm. of uric acid was dried to constant weight, samples of the dried yeast were heated repeatedly in buffer at 100° C. to extract the uric acid, and the extracts were analysed with purified uricase by the method of Kalckar[3]. It was found that the dried yeast contained 16 per cent uric acid by weight and that 35 per cent of the uric acid administered was recovered in the extracts. It is presumed that the remaining 65 per cent of the uric acid had been metabolized via the yeast uricase. The wet yeast contained 82 per cent water, so that the concentration of uric acid would be about 35 mgm./ml. of water in the wet yeast. The solubility of uric acid is given as 2·53 mgm. 100 ml. at 20° C. (ref. 4) and therefore the presence of crystalline uric acid in the yeast cell would be expected with the high concentrations that were observed.

Microscope examination of yeast cells that had accumulated purines revealed the presence of crystals in the vacuole. These were most evident in the case of *iso*guanine, which crystallized within the cell in needles that usually lay along the long axis of the cell and appeared to extend from wall to wall. To confirm the presence of purine crystals, yeast containing the various purines was treated with dilute silver nitrate to form the silver purines, washed, and treated with dilute sodium sulphide. The crystals became more striking because of blackening due to the formation of silver sulphide on the crystal surfaces; this was not observed with control yeast. Finally, when examined in the crossed field of a polarizing microscope, the crystals were seen as dots or lines of light that exhibited a twinkling effect due to Brownian movement in the case of smaller crystals. Cells that had not taken up purines remained dark in the crossed field.

It was found previously that the accumulated purines with the exception of *iso*guanine were slowly metabolized by the yeast[1,2]. Since it was considered possible that the presence of the crystals within the cell might disrupt the internal structure and interfere with normal growth, cells that contained *iso*guanine crystals or amounts of crystalline uric acid that occupied much of the vacuole were placed on nutrient agar on microscope slides and observed during the course of a day. Normal buds formed and grew from the cells containing either crystalline *iso*guanine or uric acid. Thus, it appears that growth and metabolic processes occur when the crystals are present, and it is evident that the uric acid crystals must slowly re-dissolve and be metabolized, because uric acid gradually disappears from the cells[1]. It is of interest to note that the accumulation of S-adenosylmethionine in the vacuole of *C. utilis* occurs without the appearance of crystals[5].

The crystallization of purines in *C. utilis* provides a useful system for the study of crystallization and crystal growth and dissolution processes within the living cell. The effect of purine crystallization on the active transport of the purines and on the induced formation of enzymes of purine metabolism in yeast is being studied. This investigation was supported by Research Grant CY2510 from the National Cancer Institute, National Institutes of Health, U.S. Public Health Service.

Allan H. Roush

Department of Biology,
Illinois Institute of Technology,
Chicago, Illinois.

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Plasma Clot Dissolution by Urea Derivatives

A method for forming standard human plasma clots has been described in a previous communication[1]. This method allows an accurate measurement of the clot-dissolving activities of various compounds applied in solution to a standardized invariable surface. In this previous work it was found that when a plasminogen activator, such as urokinase, was applied to the preformed clot, it produced a progressive fibrinolysis. Afterwards it was observed that the presence of 'Tween 20' in the activator solution enhanced the activator-induced fibrinolysis. The question then arose as to whether or not denaturation of fibrin by any compound would enhance the fibrinolytic process. The first group of compounds studied, and that reported in this communication, was urea and urea derivatives. Urea, itself, is a well-known denaturing agent. It enhances proteolysis in lesser concentrations[2] and dissolves fibrin in greater concentrations[3].

All compounds studied with the standard clot were dissolved in human defibrinated plasma at various concentrations. These plasma solutions were then applied to the preformed standard clots (obtained by recalcifying of plasma) either in the presence of various concentrations of urokinase or in the absence of urokinase. The progress of the clot lysis at 37° C. was noted at intervals and expressed as percentage of clot lysed.

A number of urea derivatives were found which enhanced the urokinase-induced fibrinolysis of the preformed standard clots. The degree of enhancement of the urokinase-induced fibrinolysis was not the same for each compound. Among the compounds examined were ethyl urethan, methyl urethan, allylthiourea, urethan and urea. They are listed in order of activity with ethyl urethan showing the greatest enhancement and urea showing the least. The presence of ethyl urethan, methyl urethan and allylthiourea, at concentrations as low as 2 per cent, in solution with an ineffective amount of urokinase, still promoted fibrinolysis.

Controls for experiments using concentrations greater than 2 per cent revealed that some of the derivatives were dissolving the preformed plasma clot in the absence of urokinase. The effective concentrations were considerably lower than the

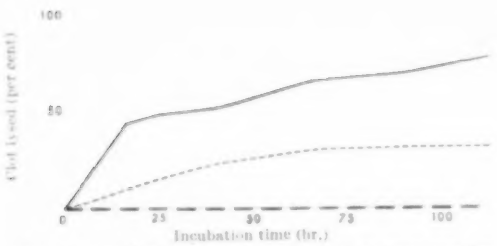

Fig. 1. Rate of dissolution of human plasma standard clots by urea and urea derivatives. ——, 0·4 *M* ethyl urethan; – – –, 0·4 *M* methyl urethan; · · · ·, 0·4 *M* urethan; ——, 0·4 *M* urea

urea concentration required to dissolve fibrin clots. Fig. 1 shows a typical example of the dissolution of preformed plasma clots by urea derivatives in the absence of urokinase.

In the experiment represented in Fig. 1, urea and urethan were ineffective. It showed that the introduction of a methyl group into the urethan molecule, however, produces a clot-dissolving substance. Still greater clot-dissolving activity is obtained with the introduction of an ethyl group.

Further work with ethyl urethan revealed that plasma could be clotted after the addition of ethyl urethan in concentrations of 3 per cent or less. As with the preformed clots, it was noted that the fibrinolysis-inducing activity of urokinase is considerably enhanced under these conditions by the presence of ethyl urethan. An example of this is shown in Table 1, where ineffective concentrations of both urokinase and ethyl urethan are combined to produce lysis in a relatively short time.

Table 1. Enhancement of Urokinase Activity by Ethyl Urethan in Human Citrated Plasma
(All clots were formed with thrombin)

Plasma plus urokinase, 15 μgm./ml.	Plasma plus ethyl urethan, 0·5 per cent	Plasma plus urokinase, 15 μgm./ml., and ethyl urethan, 0·5 per cent
No lysis in 24 hr.	No lysis in 24 hr.	Lysis in 90 min.

When 2 or 3 per cent of ethyl urethan was incorporated into plasma clots, in the absence of urokinase, it dissolved the clot within a period of 16–30 hr. This 'chemical' lysis occurred regardless of the clotting technique (spontaneous, recalcification, or thrombin). Representative examples of dissolution of clots spontaneously formed in the presence of ethyl urethan are shown in Table 2. The human plasma was obtained by the silicone technique and afterwards permitted to clot in glass tubes. A firm clot was produced in each case.

Table 2. Dissolution of Human Plasma Clots formed spontaneously in the Presence of 2 per cent Ethyl Urethan

	Clotting time (min.)	Clot dissolution time (hr.)
Plasma *A*	15	23
Plasma *B*	19	22
Plasma *C*	10	30

As a working hypothesis and in analogy with the well-known protein-dissolving properties of higher urea concentrations, it is thought that ethyl urethan and other urea derivatives weaken the fibrin network by denaturation (breaking of hydrogen bonds). Denaturation is known to facilitate enzymatic hydrolysis. It has also been suggested that denaturation is a pre-requisite of any enzymatic degradation of proteins[4]. This would explain the marked enhancement of urokinase-induced fibrinolysis by these urea derivatives. This concept might also hold true for clots formed in the presence of ethyl urethan, but in the absence of urokinase which undergo subsequent dissolution. In this case the fibrin denaturation could have been carried to a point which permitted the endogenous 'masked' fibrinolytic activity of plasma[5] to dissolve the fibrin. We also have suggestive evidence that the urea derivatives described actually activate plasma plasminogen in the presence of the plasma factor (pro-activator ?)[6].

Urea at 30 per cent dissolves fibrogen clotted by thrombin, but does not dissolve clots formed in the presence of a stabilizing serum factor and calcium[7]. Urea was ineffective at the concentrations used in this study of urea derivatives. The urea derivatives found to dissolve plasma clots did so regardless of the method used for clotting and at concentrations of 2 or 3 per cent. This indicates that the mode of action of these compounds is quite different from that of urea.

There were relationships between the chemical structure of the derivatives and their clot-dissolving power. This relationship could be a useful starting point in the search for more powerful 'chemical' clot-dissolving agents. Further work is in progress in our laboratories.

This work was supported by a grant-in-aid from the American Heart Association.

Kurt N. von Kaulla
Robert L. Smith

Department of Medicine,
University of Colorado School of Medicine,
and Belle Bonfils Memorial Blood Bank,
Denver, Colorado.

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Clotting-Time of Cold-exposed and Hibernating Hamsters

Prolonged blood-clotting in hibernating hamsters has been reported by Svihla *et al.*[1]. In another experiment with ground squirrels[2], it was concluded that the prothrombin-level decreased during hibernation, but the use of the one-stage prothrombin test for calculating prothrombin concentrations is questionable[3]. Suomalainen and Lehto[4] found that both naturally and artificially dormant hedgehogs had an increased clotting-time and increased heparinocyte counts of the small intestine and bronchioles.

The Syrian hamster (*Mesocricetus a. auratus*) requires several weeks of exposure to cold before entering hibernation. As a result, it has been possible to ascertain whether an increased clotting-time occurs gradually during the weeks of acclimation or is a phenomenon immediately preceding hibernation.

The hamsters were kept in a cold room at 5 ± 1° C. for varying periods of time. Each group contained ten animals, except for the hibernating group in which there were three animals. Each hamster had a separate cage with 'Purina' laboratory chow and water *ad libitum*. The first group lived in the cold

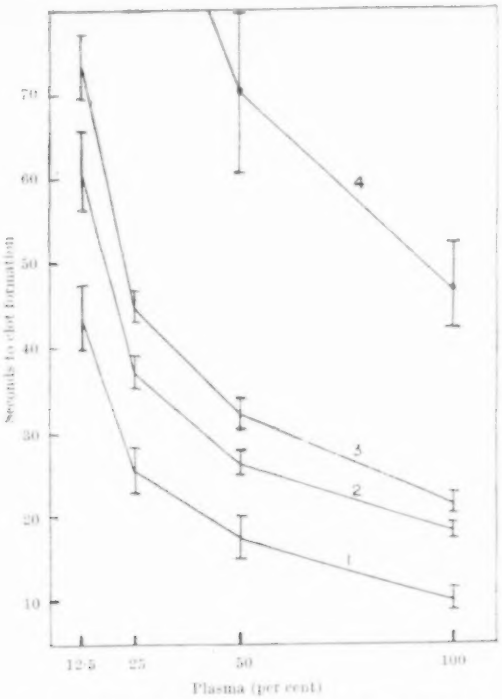

Fig. 1. Clotting-time with Russell's viper venom of various dilutions of plasma from hamsters exposed to cold (5 ± 1° C.) for (1) no weeks, (2) two weeks, (3) eight weeks, and (4) in hibernation

for 2 weeks, the second group for 8 weeks, and the hibernating animals had been in the cold for 12 or more weeks. The control animals were taken from the stock room at 22 ± 1° C. The animals were lightly anæsthetized with nembutal and the blood taken by cardiac puncture into a siliconed needle and syringe. The clotting times of 100, 50, 25 and 12·5 per cent plasma were determined in siliconed glassware at 37° C., using Russell's viper venom for the one-stage prothrombin time test.

In Fig. 1 the means of each group at the various dilutions of plasma are plotted with the vertical lines representing the standard errors. The Russell's viper venom time increased for each dilution as the cold exposure time of the animals increased. The increases in clotting-time from group to group for the various dilutions are relatively similar except for the hibernators. By 8 weeks of cold exposure the clotting-times are approximately between those of the control group and the hibernating group. This indicates that there has been a steady increase or decrease in some component of the plasma which affects the efficiency of Russell's viper venom. According to Fullerton and Anastasopoulos[5], Russell's viper venom is relatively insensitive to alterations in plasma prothrombin. De Beer[6] has shown that viper venom reveals both the intensity and duration of the anticoagulant activity of heparin. Therefore, the increased clotting-time of Fig. 1 cannot be explained as a reduction in prothrombin only and may reveal an increase in heparin.

The heparin content of the blood from control hamsters and hamsters exposed to cold (5 ± 1° C.) for 8 weeks was determined by a protamine titration

Table 1. CLOTTING-TIME OF 100 AND 25 PER CENT PLASMA WITH RUSSELL'S VIPER VENOM AND THROMBOPLASTIN AND THE HEPARIN CONCENTRATION OF THE PLASMA OF HAMSTERS EXPOSED TO COLD (5 ± 1° C.)

Weeks in the cold 5 ± 1° C.	No. of animals	100 per cent plasma		25 per cent plasma and thromboplastin	
		Venom clotting-time (sec.)	Thromboplastin clotting-time (sec.)	Normal clotting-time (sec.)	Plasma heparin (γ/ml.)
0	8	14·1 ± 1·8	14·5 ± 1·4	23·6 ± 4·0	7·4 ± 1·4
8	7	25·1 ± 2·7	18·9 ± 3·2	22·4 ± 2·5	14·0 ± 1·6
12 (Hibernating)	3	47·3 ± 5·5	30·0 ± 4·5		

technique[7]. The test was modified by adding 5γ rather than 10γ of exogenous heparin (Connaught Laboratories) to the plasma. The results are summarized in Table 1. The concentration of heparin, as measured by this test, was increased twofold in the blood of hamsters exposed to cold for eight weeks. With 100 per cent plasma there was no significant difference in the clotting-time between the venom and brain thromboplastin. After 8 weeks in the cold, the clotting-time was more prolonged with venom but not with thromboplastin. The clotting-time of 100 per cent plasma as determined previously on hibernating hamsters was very significantly increased with both venom and thromboplastin. With 25 per cent plasma and thromboplastin, there was no increase in the clotting-time at 8 weeks, although as seen from Fig. 1 there was a significant increase at this dilution with venom. Some plasma component to which Russell's viper venom, but not thromboplastin, is very sensitive significantly altered in 8 weeks of cold exposure.

Clotting-time with Russell's viper venom is affected by the concentration of plasma lipid, and plasma deprived of lipid will not clot with this venom[8]. In view of this, the present results indicate that the concentration of plasma lipid altered during the prolonged cold exposure. This lengthened the clotting-time with the venom and had only a slight effect on the activity of brain thromboplastin. The accompanying increase in plasma heparin is probably related to the change in plasma lipid since heparin is believed to be involved in fat transport[9]. The highly significant increase in clotting-time during hibernation probably arises from a combination of reduced prothrombin synthesis, resulting from a general lowering of body metabolism, and a high concentration of some heparinoid substance in the plasma.

This work was aided by a grant from the Society of Sigma Xi.

ARLISS DENYES
JOAN D. CARTER

Biology Department,
Queen's University,
Kingston,
Canada.

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Bile Pigment Excretion in Amphibia

In man and in other mammals, bilirubin is excreted in conjugated form, mainly as the glucuronide. Since in mammalian foetal liver the enzymatic mechanism for glucuronide formation is poorly developed, reaching its full capacity only after birth, transient hyperbilirubinæmia is frequently observed during the neonatal period[1]. In the amphibian genus, *Rana*, hepatic glucuronide formation is absent in the larva, but present in the adult[2]. The larval forms undergo extra-uterine development and hence are readily accessible. These Amphibia would represent an excellent experimental model for studying various aspects of neonatal hyperbilirubinæmia, if it could be established that they, like mammals, excrete bilirubin as glucuronide. Therefore, we have examined amphibian bile pigment excretion to determine, first, whether in the adult *Rana* bilirubin is excreted as a glucuronide; secondly, whether metamorphosis is associated with qualitative or quantitative changes in pigment excretion; and thirdly, whether the excreted pigment is biliverdin, as has been postulated previously[3], bilirubin, or another pigment.

Larval forms of *Rana catesbiana* and adult forms of *Rana pipiens*, *Xenopus laevis*, and *Necturus maculosus* were examined. The last two remain aquatic throughout adult-hood; in addition, *N. maculosus* fails to metamorphose while achieving sexual maturity. As expected[2], hepatic glucuronyl transferase activity was demonstrable only in adult *R. pipiens* but was lacking in the liver of the larvæ, and the two adult aquatic Amphibia (Table 1).

Table 1. Enzymatic Synthesis of *o*-Aminophenyl Glucuronide by Liver Homogenate from Amphibian Species

Species	Sex	No. of assays and incubation temperature (° C.)	*o*-Aminophenyl glucuronide formed: Average	Range
R. catesbiana, larvæ	M, F (pooled)	2; 21	not demonstrable	
R. pipiens, adults	M	6; 37	0·363	0·279–0·412
		6; 21	0·290	0·260–0·344
X. laevis, adults	M	4; 37	not demonstrable	
		2; 21	not demonstrable	
N. maculosus, adults	M	2; 37	not demonstrable	
		2; 21	not demonstrable	

Liver was homogenized with 5 parts of 0·154 *M* potassium chloride. 1 ml. of homogenate was incubated for 30 min. in air with 30 μM magnesium chloride, 1·0 μM uridine diphosphate glucuronic acid, 0·125 μM *o*-aminophenol and 0·1 ml. 0·5 *M* phosphate buffer *p*H 8·0; final incubation mixture was 1·5 ml. (ref. 6). Results are expressed in μmoles per gm. of liver.

The gall-bladder bile of adult *R. pipiens* invariably contained bilirubin (Table 2) and frequently biliverdin[4], but on paper chromatographic analysis[5] bilirubin glucuronide could not be demonstrated. The bile of *X. laevis* and *N. maculosus* usually exhibited high concentrations of bilirubin (Table 2) and occasionally some biliverdin. The bile of *R. catesbiana* larvæ, though yellow or green in colour, contained only trace amounts of bilirubin and biliverdin and gave a negative Gmelin reaction. Similarly, in adult *R. pipiens*, *X. laevis* and *N. maculosus*, but not in larvæ of *R. catesbiana*, urobilinogen was present in the intestinal tract. The serum of all adult species examined was colourless or only faintly yellow. Larval serum, on the other hand, was intensely yellow with peak absorption at 4600 Å., suggesting the possible presence of bilirubin. The diazo reaction, however, gave only insignificant spectrophotometric readings, and it was not possible to establish that the yellow pigment was a bilirubinoid compound.

Table 2. Bile Pigments in Amphibian Bile and Intestinal Content

Species	Gall bladder: Weight (mgm.)	Gall bladder: Bilirubin content* μgm. per gall bladder	Intestinal urobilinogen†
R. catesbiana, larvæ	19·4–33·5	0–0·2	absent
R. pipiens, adults	17·6–42·6	9·3–47·0	present
X. laevis, adults	72·6–75·8	1·6–43·0	present
N. maculosus, adults	198·0–230·0	53·0–54·0	present

* Bilirubin was determined by the diazo reaction (ref. 7).

† Urobilinogen was identified spectroscopically with *p*-dimethylaminobenzaldehyde (ref. 4).

These observations indicate that, in adult Amphibia, biliary excretion of bile pigment is independent of the presence of a functioning mechanism for glucuronide formation. Moreover, in adult *R. pipiens* no evidence was obtained for excretion of bilirubin as a glucuronide, even though glucuronyl transferase is present in the liver. In larvæ, the finding of yellow serum, the virtual absence of bilirubin and biliverdin in the bile, and the absence of urobilinogen from the intestinal tract suggest a mode of bile pigment excretion different from that in adult animals. Finally, in contrast to earlier reports[3], the bile of all adult animals contained bilirubin while biliverdin could not be demonstrated in all instances.

This work was supported in part by U.S. Public Health Service grant A-1833.

Roger Lester
Rudi Schmid

Thorndike Memorial Laboratory,
Second and Fourth (Harvard) Medical Services,
Boston City Hospital,
and
Department of Medicine, Harvard Medical School,
Boston, Mass.

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Fractionation of the Motor Unit during Repetitive Response to Prostigmine

Recent work has demonstrated fractionation of the action potential of the single motor unit of the rat gastrocnemius into anatomically unidentified sub-units[1]. The temporal sequence of firing of these sub-units can be altered by intravenous administration of curare or decamethonium. These drugs, by reducing the end-plate potential, increase the latency of appearance of the propagated spike of some, but not all, of the sub-units which comprise the action potential of the single motor unit. When the time of rise for the end-plate potential of the sub-unit is sufficiently prolonged, the propagated spike of the sub-unit disappears[2], and the total unit potential is reduced. In order to evaluate the effect of prostigmine on the single motor unit, the work reported here was undertaken.

Under intraperitoneal sodium pentobarbital anæsthesia, laminectomy was performed in 18 male albino rats, weighing 250–400 gm. With binocular magnification of × 25, a ventral root innervating the gastroc-

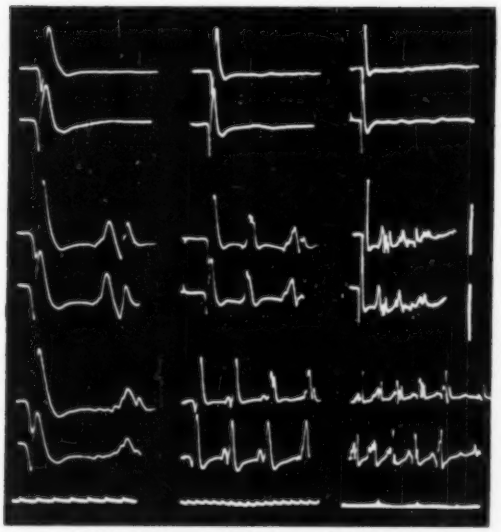

Fig. 1. Response of motor unit to prostigmine. Upper pair of traces, control responses of single motor unit of gastrocnemius to single stimulus delivered to ventral root filament. Middle and lower pairs of traces, random trains following intravenous administration of 0·02 mgm. prostigmine. Rhythmic repetitive responses to a single stimulus delivered to a ventral root filament occur at 4 msec. intervals. The second and subsequent responses reveal decreased amplitude and increased duration secondary to the asynchrony of firing of the 'sub-units'. Time: cols. 1 and 2, 1 msec.; col. 3, 10 msec. Calibration, 0·1 mV. upper channel; 0·2 mV. lower channel

nemius was separated from the spinal cord and teased into fine filaments, one of which was stimulated with a rectangular pulse of 0·02–0·05 msec. delivered from a Grass 3C stimulator. A single motor unit on the surface of the gastrocnemius was identified with two pairs of bipolar recording electrodes made of enamel-insulated copper wire of 140μ diameter, was amplified with a low-level a.c. pre-amplifier and displayed on a dual-beam oscilloscope. Spinal cord, nerve roots and gastrocnemius were maintained at body temperature in small mineral oil pools. The presence of a single unit was determined by a sharp threshold of stimulus strength, below which no response appeared, and above which response form remained unaltered. A series of control responses was photographed at a stimulus strength of at least three times threshold, and intravenous prostigmine methylsulphate was administered in doses of 0·012–0·0375 mgm. The response of the motor unit was followed photographically every 3–6 sec.

Within 38–150 sec. following administration of the drug, multiple responses to the single stimulating shock appeared (Fig. 1). The second and subsequent responses showed fractionation of the action potential of the single unit into component sub-unit potentials, similar to the fractionation that had been demonstrated in the single response to a stimulus following administration of a blocking agent. The duration of the initial response remained at control value following administration of prostigmine; the amplitude of the initial response either remained at control value or increased to a maximum of 27 per cent (Fig. 1, channel *A*) until late in the experiment when a fall of amplitude was ascribed to deterioration of the preparation.

In three animals doses of prostigmine ranging from 0·25 to 1·0 mgm. were used. Repetitive responses failed to appear following this larger dose, and no change in duration or form of the motor unit response occurred. Fasciculation of the gastrocnemius was always visible at the time of onset of repetitive responses, but was not apparent following the larger dose of prostigmine.

Repetitive response of eserinized muscle was described by Brown[3], and has been thought to result from prolonged local potentials at the end-plate[4]. Riker *et al.*[5], and more recently Werner[6], have suggested the repetitive response of muscle to a single impulse in nerve results from the physiological independence of the nerve terminals. Following administration of quaternary ammonium derivatives or physostigmine, single or repetitive post-synaptic orthodromic responses were associated with repetitive antidromic axonal responses. These authors suggest initiation of the repetitive activity at the nerve terminal. The present findings, which demonstrate fractionation of the repetitive responses, would indicate either that the generation of repetitive impulses in the nerve terminals following administration of prostigmine is asynchronous, or that the effect of the drug on the subneural apparatus of a single motor unit permits asynchronous firing of the sub-units. The nature of the sub-unit is still unknown.

This work was supported in part by the Myasthenia Gravis Foundation, Inc.

SIMEON LOCKE

Neurological Unit,
Boston City Hospital,
and
Department of Neurology,
Harvard Medical School,
Boston, Mass.

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Effect of Artificial Fever in Increasing Susceptibility to Bacterial Endotoxin

THERE is remarkably little information concerning the effect of fever on mechanisms of resistance to infection[1]. Indications of a potentiating effect of high ambient temperatures on mortality in mice challenged with endotoxin or with Gram-negative bacilli have been recorded[2–4]. Recently, Bannister[3] has observed that high ambient temperatures potentiate the febrile response to pyrogenic doses of endotoxin in human volunteers. Burack has observed that the Shwartzman response in the skin of rabbits is also conditioned by the environmental temperature[6]. Work on the effect of environmental temperature on the lethality of endotoxin was therefore undertaken.

Webster Swiss strain mice, weighing 9–12 gm., were given graded doses of *S. typhosa* endotoxin intraperitoneally. The endotoxin, extracted as previously described[7], was dissolved in sterile saline. No striking sex difference in susceptibility to endotoxin was observed. However, in each experiment mice of a single sex were used. When mice were maintained in an air-conditioned room at 22° C.,

the LD_{50} of the endotoxin varied between 400 and 800 μgm. When mice were placed in a well-ventilated incubator at 37° C. for 24 hr., and then given endotoxin and placed back at 22° C., the LD_{50} was not significantly altered (Table 1). Mice that were maintained at 22° C., given endotoxin and placed immediately at 37° C., had an LD_{50} of but 21 μgm. (range 11–23 μgm. in repeated experiments). Mice pre-incubated at 37° for 24 hr., given endotoxin and then returned to the 37° C. environment had an LD_{50} of less than 1 μgm. Deaths were not observed in control animals injected with saline and maintained at either temperature. Thus, the effect of raising the ambient temperature was to increase susceptibility to the lethal action of endotoxin.

Table 1. Effect of Environmental Temperature on Lethal Action of Bacterial Endotoxin in Mice*

Environmental temperature		
Pre-injection	Post-injection	LD_{50} (μgm.)
22° C.	22° C.	500
37	22	732
22	37	21
37	37	< 0·96

* Female mice weighing 9–12 gm.

The mode of death differed in accordance with the environmental temperature. At 22° C. there was a lag period of several hours, with no apparent evidence of distress, followed by increasing tremulousness and gradual suppression of activity, with death occurring 12–18 hr. after administration of endotoxin. At 37° C., on the other hand, mice appeared quite well for 2–4 hr., then suddenly developed convulsive seizures with collapse and death occurring shortly thereafter.

In order to determine the effect of environmental temperature on the body temperatures of the animals, rectal thermistor probes in fine plastic catheters were inserted, and the mice were restrained from interfering with the probes by immobilization in loose envelopes constructed of ¼-in. open-mesh plastic screening. These envelopes permitted a moderate amount of muscular activity and free exposure to the ambient air. Temperatures were recorded every 15 min. using an electronic recorder, and observations were made for three hours.

Hypothermia was invariably observed in mice kept at 22° C. and given endotoxin, as has been observed by others[8]. Uninjected mice varied in body temperature but consistently increased their body temperatures when placed in an incubator at 37° C. The increased body temperature was sustained during the three hours of incubation, reaching a maximum at about 1 hr. and remaining relatively constant thereafter. However, when mice were given a large dose of endotoxin (1 mgm. per mouse) and placed at 37°, the febrile response was invariably greater than that observed in control animals given saline and kept at the same temperature. Similarly, mice that were given endotoxin after having been kept in the incubator for two hours underwent a still further rise in temperature during the next few hours, whereas animals given saline alone maintained relatively constant temperatures with continued incubation. About 2/3 of the animals receiving 1 gm. of endotoxin died during the 3-hr. period of observation at 37° C., and deaths coincided with rapid elevation of body temperatures to values greater than 41·5° C.

These experiments indicate: (*a*) that elevation of environmental temperature increases susceptibility to the lethal action of endotoxin; (*b*) that careful control of body temperature in experiments employing lethal doses of endotoxin is essential; (*c*) that mice may develop fever when given endotoxin if their body temperatures have initially been elevated; (*d*) that the increased susceptibility to endotoxin and the sudden death seem to be related to the increased body temperature of the host animal.

David G. Connor
Edward H. Kass

Boston City Hospital
and
Harvard Medical School,
Boston, Mass.

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HÆMATOLOGY

A New Hæmoglobin Variant (the 'Honolulu Type') in a Chinese

Recently several hæmoglobin variants have been described with electrophoretic mobilities between those of hæmoglobins *G* and *S* in paper electrophoresis, veronal buffer, *p*H 8·6, namely, types *L* (ref. 1), *P* (refs. 2 and 3), and Stanleyville I (refs. 4 and 5). One case of hæmoglobin *G* was found in a Chinese[6]. The present report deals with a new hæmoglobin variant in a Chinese, similar to *L*, *P* and Stanleyville I in paper electrophoresis, but distinguished from them by chromatography or free electrophoresis.

The variant was found in a forty-three-year-old unmarried woman, J. C., a resident of Honolulu, whose condition was termed 'anæmia' by a local physician about three years ago. The initial red blood cell count was 4·5 million per mm.^{3} and the hæmoglobin 10·4 gm. per cent; after iron therapy the red cell count increased to 6·0 million and the hæmoglobin to 12 gm. per cent. About seven months ago, J. C. consulted another physician for the complaints of

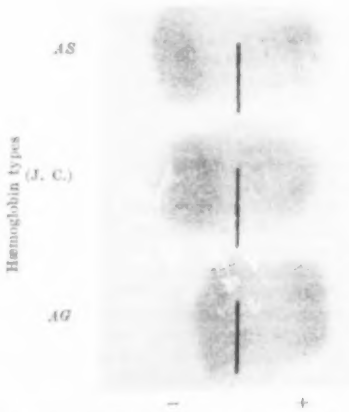

Fig. 1. Paper electrophoresis pattern of J. C.'s hæmoglobin sample compared with *AS* and *AG*, veronal buffer, *p*H 8·6, μ 0·05

Fig. 2. Chromatography of haemoglobin of J. C., 'Amberlite *IRC*-50', citrate buffer, *p*H 6·0, compared with *A2S* control

fatigue, pruritus ani, and anxiety; at that time sternal bone marrow puncture revealed active erythropoiesis, with normally cellular marrow, but deficient in iron stores. Two months later (after iron therapy) she was examined by one of us (R. T. S. J.), who obtained the following laboratory data: red blood cells, 4·8 million, haemoglobin 12·6 gm. per cent, reticulocytes 1 per cent (Dameshek method), with slight anisocytosis, poikilocytosis, occasional microcytic hypochromic cells and occasional target cells. The serum bilirubin value was 0·3 mgm. per cent total and 0·1 mgm. per cent indirect. Coombs tests, both direct and indirect, were negative. The quantitative osmotic fragility curve showed a shift to the right, beginning at about 0·45 and being completed at about 0·2 per cent sodium chloride. There were no noteworthy findings on physical examination.

In paper electrophoresis, veronal buffer, *p*H 8·6, J. C.'s haemoglobin sample resolved into two components (Fig. 1), one identical with haemoglobin *A* and the other moving between haemoglobins *G* and *S*. In chromatography on 'Amberlite, *IRC* 50', citrate buffer, *p*H 6·0 (ref. 7), J. C.'s haemoglobin sample slowly separated into two components, one identical with haemoglobin *A* and the other similar to *S*, but slightly faster, and with considerable 'tailing' towards *A* (Fig. 2). In contrast, haemoglobin *L* moves between *S* and *C* in this method, and *P* does not separate from *A*, while Stanleyville I is indistinguishable from *S*.

In free electrophoresis, cacodylate buffer, *p*H 6·5, μ 0·1, J. C.'s haemoglobin sample migrated as one sharp peak. In a 1 : 1 mixture of this sample with one from a patient with sickle-cell anæmia there developed two poorly separated components with 63 per cent in the leading one. This electrophoretic behaviour is similar to that previously observed for haemoglobin *AP*; in contrast, Stanleyville I moves like *S* in this method.

In electrophoresis in agar gel, citrate buffer, *p*H 6·0 (ref. 8), J. C.'s haemoglobin sample moved like haemoglobin *A*; however, when large amounts of sample were applied, to the extent of 'overloading', there were two components, like *A* and *G* respectively. In quantitative estimations of this sample in starch block electrophoresis, veronal buffer, *p*H 8·6, the percentage of haemoglobin *A* and of the variant were approximately equal, and that of haemoglobin A_2 was 1 per cent or less. In the method of alkali denaturation[9], the *F* haemoglobin value was 1·5 per cent. Unfortunately, no other members of J. C.'s family were available for study.

In summary, a new haemoglobin variant, appearing together with haemoglobin *A*, has been found in a Chinese woman living in Honolulu. It was not accompanied by any distinctive clinical or haematological findings. This variant resembles types *L*, *P* and Stanleyville I in zone electrophoresis, veronal buffer, *p*H 8·6. It differs from *L* and Stanleyville I in free electrophoresis, cacodylate buffer, *p*H 6·5, μ 0·1, in which method, like haemoglobin *P*, it does not separate from *A*. It differs from haemoglobin *P* (and from *L*) in chromatography on 'Amberlite *IRC* 50', in which it resembles (but is slightly faster than) Stanleyville I. It is suggested that this variant be provisionally designated the 'Honolulu type'.

This work was supported by U.S. Public Health Service Grants *A*780, *H*3189 and *H*3480.

ROSE G. SCHNEIDER

Tissue Metabolism Research Laboratory,
University of Texas Medical Branch,
Galveston, Texas.

ROBERT T. S. JIM

Professional Center Building,
Honolulu, Hawaii.

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The *Gm*^{a} Factor in Japanese

A NUMBER of blood group antigens in addition to hair, eye, and skin colours, the shape of teeth, fingerprints and palm-patterns, ear wax, etc., are used as markers in anthropological research.

Grubb[1] showed that certain human sera when added to the serum of certain rheumatoid arthritis patients will inhibit the agglutination of group $O\,Rh_0(D)$ positive cells sensitized with selected incomplete anti-$Rh_0(D)$ antibody. The human sera having a factor inhibiting the agglutinating activity of rheumatoid arthritic serum were named *Gm*(*a* +) and others which do not, *Gm*(*a* −). It is believed that the *Gm* factor exists in the γ-globulin fraction.

The studies of the *Gm*^{a} factor have been made by various workers and the frequency of *Gm*(*a* +) individuals among the white population was about 40–60 per cent. However, Grubb *et al.*[2] recognized 95 per cent of 74 Eskimos to be *Gm*(*a* +), Moullec *et al.*[3] reported that all of 500 African Negroes were *Gm*(*a* +), Steinberg *et al.*[4] found 98 per cent of 98 American Negroes to be *Gm*(*a* +), and Steinberg

et al.[5] observed that all of 89 American Indians were $Gm(a+)$.

Since it was already well known that the blood-group frequencies of Japanese vary from those of other populations[6,7] it seemed possible that the distribution of the Gm^a factor might also manifest a detectable deviation.

We tested for the Gm^a factor employing rheumatoid arthritis serum, $Gm(a+)$ and $Gm(a-)$ control sera obtained through the courtesy of Dr. R. Grubb, Bacteriological Institute, Lund, Sweden, together with two anti-$Rh_0(D)$ sera selected for their suitability from the specimens which had been stored by one of us (M. Y.) at the Blood Typing Laboratory and Rh Center, Tokyo Medical and Dental University. Later, we received a suitable anti-$Rh_0(D)$ serum from Dr. A. Eyquem, Pasteur Institute, France.

The agglutination-inhibition test (Gm^a grouping) was carried out according to the method of Grubb and Laurell. The tests were performed on 816 normal human sera with the following results: Only 2 (1·0 per cent) of 200 random blood donors in Tokyo and 13 (2·4 per cent) out of 616 blood donors in Kumamoto were found to be $Gm(a-)$. Conversely, we found approximately 98–99 per cent of these sera to be $Gm(a+)$ and the serum factor to be inherited as a dominant Mendelian character (Table 1). In addition, a study was carried out on 34 families whose progeny included identical twins. The test was performed only on the sera of the parents and the twins for a total of 136 tests. Five individuals were found to be $Gm(a-)$. This included 1 parent from each of 4 families and 1 twin from one of these 4 families. Gm^a serum grouping together with other genetic investigations are still being conducted on the family in which one of the identical twins and one of the parents were $Gm(a-)$.

Table 1. The Gm^a Factor in Japanese

No. tested	Gm^a factor $Gm(a+)$ (per cent)	$Gm(a-)$ (per cent)
816	801 (98·13)	15 (1·87)
136*	131 (96·32)	5† (3·68)

* From family study on twins (34 families).
† In four families.

As new blood groups are found and their frequencies determined, it seems probable that additional racial differences will be noted in their distribution. The Gm^a factor together with Gm^x, Gm^b and Gm-like factors should prove also to be useful tools in anthropological research.

We wish to acknowledge the kind assistance of Dr. R. Grubb and Dr. A. Eyquem in this work.

M. Yokoyama*
The Blood Typing Laboratory and Rh Center,
Tokyo Medical and Dental University,
Tokyo.

N. Ueno
Kaketsuken Blood Bank,
Kumamoto, Japan.

* Present address: Division of Biologics Standards, National Institutes of Health, Bethesda 14, Maryland, U.S.A.

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The γ-Globulin, Gm^{ab}, in Nigerians

The γ-globulin (*Gm*) genetic polymorphism, first described by Grubb[1], exhibits considerable geographical variation. Steinberg, Boyer and Stauffer[2] recently observed a striking excess of the phenotype *Gm* $(a+b+)$ among Negroes in the United States. Accordingly it was suggested that an allele, Gm^{ab}, exists in coloured populations. The allele frequency of Gm^{ab} among 593 Negroes from Maryland and Ohio is 0·690. The difference between this value and unity was taken as an estimate of European genetic admixture in American Negroes. Essential to this estimate was the assumption that Gm^{ab} frequency is nearly 1·00 in native West Africans. Moullec[3] had previously reported that 449 residents of Dakar were all $Gm(a+)$; however, typing of *Gm b* was not then possible and has not since been described in a West African population.

In the present work aliquots of serum or whole blood from 409 native Nigerian blood bank donors was forwarded, by air, from Ibadan to the United States. *Gm a* and *Gm b* were detected in the manner previously described[4].

All individuals were clearly *Gm* $(a+b+)$. There is a probability of 0·05 that either Gm^a or Gm^b is present with an allele frequency of 0·05 but was, by chance, omitted from the present survey. The assumption that Gm^{ab} has a frequency of near unity in West Africans is consequently confirmed.

This work was supported in part by United States Public Health Service Grant No. *B2053* from the National Institute of Neurological Disease and Blindness.

Samuel H. Boyer
Division of Medical Genetics,
Department of Medicine,
The Johns Hopkins University and Hospital,
Baltimore.

E. J. Watson-Williams
Department of Pathology,
University College Hospital, Ibadan.

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PATHOLOGY

Surface Enamel Magnesium and its Possible Relation to Incidence of Caries

Following the semi-empirical administration of a mixture of alkaline phosphate to a group of 200 patients during a period of three years, it has been noticed that the incidence of caries on continuous enamel surfaces has been significantly inhibited at all age-levels. The surface enamel of exfoliated or extracted teeth from these and other patients is being investigated, and the magnesium content has been shown to vary within extremely broad limits.

This magnesium variable has been correlated with caries incidence or inhibition, also with an abrasive or non-abrasive prophylaxis, and finally, with a (possibly) minerally deficient diet or with a minerally enriched diet. The mixed mineral salts supplied were 50 per cent magnesium phosphate, 25 per cent calcium phosphate and a small percentage of potassium, sodium and iron phosphates. They were fluoride-free.

Table 1. Analytical Results, corrected to 0·0050 gm. Sample, Expressed in ml. 0·002 *M* Ethylenediamine Tetraacetic Acid (First Series 29/3/60)

Patient	Age (yr.)	Tooth	Dental status	History	Calcium	Magnesium
P.C. (female)	11	Lower right permanent canine	Non-carious, non-abraded	Magnesium salts, 2 yr., inhibited caries incidence	4·73	0·22
R.R.* (female)	11	Right lower deciduous second molar	Non-carious, non-abraded	Magnesium salts, 8 yr., inhibited caries incidence	4·33†	0·13
L. (male)	30	Left upper first molar	Three enamel surfaces intact	Abrade-! regular toothpaste, caries-prone, non-salts	4·75	0·03
P.W. (male)	25	Upper permanent canines	Carious distally ; labial, lingual surfaces intact	Abraded regular toothpaste, caries-prone, non-salts	4·6	0·05
A.C. (female)	5	Lower deciduous centrals	Non-carious, non-abraded	Magnesium salts, inhibited caries incidence	3·65†	0·42
D.B. (female)	8	Lower right permanent central	Non-carious	Abraded toothpaste *C*‡, orthodontic removal, non-salts	4·75	0·19
A.M. (male)	12	Upper deciduous canines	Non-carious, non-abraded	Magnesium salts, inhibited caries incidence	4·19†	0·49
F.G. (male)	10	Upper left deciduous molar	Well filled three intact surfaces collectively non-abraded	Magnesium salts, 2 yr., inhibited caries incidence	4·35	0·30
Mrs. T.	28	Upper right canine	Non-carious, non-abraded	321 123 pyorrhœa alv., intact enamel, otherwise edentulous, toothpaste *C* occasionally, non-salts.	4·70	0·27
J.M. (male)	7	Upper deciduous laterals	One sound, one carious	Exfoliated, abraded, toothpaste, non-salts, caries-prone	4·42	0·08
K.K. (female)	5	Upper left lateral	Non-carious, non-abraded	Magnesium salts, 18 mnth., inhibited caries incidence	4·13†	0·28
R.R.* (female)	11	Left deciduous second molar (lower)	Non-carious, non-abraded	Magnesium salts, 8 yr., inhibited caries incidence	4·81†	0·10
S.M. (male)	12	Lower right permanent canine	Non-carious	Orthodontic removal, not completely erupted, toothpaste non-salts, caries-prone	4·60	0·14
A.C. (female)	5	Lower deciduous laterals	Non-carious, non-abraded	Magnesium salts, 2 yr., inhibited caries incidence	3·50†	0·30
— (male)	56	Lower right second premolar	Carious, buccal surface intact, smooth	Extracted for pulp-degeneration, caries-prone, non-salts	4·50	0·12

* These teeth were re-washed some months after exfoliation. Surface organic degradation may render magnesium more soluble, hence possible loss in washing.
† Organic charring noted in these samples.
‡ Tooth-paste *C* appears to be highly surface reactive, and uniquely compatible with a surface enamel preservation therapy.

Preliminary chemical analyses, carried out in the Chemistry Department, University of Otago, have indicated that an important role can possibly be assigned to magnesium (phosphate) in the stabilization of chemical, physical and electrokinetic states of the surface enamel calcium. As in all biological assays, the method of analysis has been considered of primary importance, and is reported here in detail.

All teeth, immediately after extraction, were washed and rubbed with cotton wool in distilled water, then air dried at 20° C. for several days. Intact enamel surfaces (bucco-labial and lingual) were subjected to a standardized abridement, a new No. 35 *SSW* carbide inverted cone bur, at approximately 50,000 rev./min. in a rigid handpiece, scoring a light line down the incisal (or occlusal) two-thirds of the surface at an approximate depth of 50–100μ. A series of similar, parallel lines was scarified on the area to be sampled, a measurable evenness of depth being obtained with some certainty after considerable experience. The bur was then moved lightly cross-wise against the intervening ridges, reducing the scored area to a uniform level. The very finely powdered enamel thus produced settled (in a still atmosphere) on a foot square of clean 'Polythene' covered card. This was carefully brushed into a prepared, wide-necked dry glass jar, sealed, and labelled ready for micro-sampling.

After each enamel surface was thus sampled, the bur was cleaned and inspected under a microscope for vane damage. If detected, the bur was discarded. Each sample was subjected to a high magnetic drag to remove any ferric contamination possible in this method. Samples were then submitted to water-bath dehydration for 48 hr. A varying weight of sample was micro-weighed and ashed at the minimum temperature with a drop of sulphuric acid in platinum vessels. The mineral ash was dissolved again successfully by dilute acid re-digestion and water elution into 'Polythene' receptacles, and prepared for a 'double blind' series of titrimetric analyses.

The method of Betz and Noll[1] (for total magnesium–calcium estimation) was modified. A 5-ml. sample was pipetted into a white 'Polythene' beaker. 1 ml. standard $MgSO_4.7H_2O$ (0·001 gm./l.) was added and made up to 50 ml. *p*H was adjusted to 7·0 with a glass electrode *p*H meter. 0·3 ml. freshly made standard buffer (A.R. borax, sodium hydroxide) was added, bringing the *p*H to 10·5. 0·1 mgm. 'Solochrome' indicator (standard preparation) was added and swirled until dissolved. Titration was with 0·002 *M* ethylenediamine tetraacetic acid

(disodium) under an automatically condensed light from a single Philips' 8-V. 50-W. lamp through a standard blue filter, giving an intense field of beamed white light (approximately *K* 5,500) on to white filter paper. Blue filter is not critical but the titrating light field, when photographed in daylight 'Kodachrome', should give a normal colour balance, indicating approximately light grading *K* 5,500. Light deterioration became evident only after 15 hr. service. All titrations were carried out in a dark-room, at 20° C. Titration end-point was to the definite discharge of the slightest purple tint, the final cold blue being stable over a period of at least 45 min. Continuous vigorous agitation accompanied a minimum titration time of 3 min., a rigorously standardized procedure.

As a trace of iron sometimes gave the blue colour a greyish tint, a preliminary titration of each sample gave a separate standard for colour comparison, being over-titrated 0·1 ml. to a stable blue. All analyses were double- or triple-checked, and consistent figures were obtained throughout.

Calcium estimation was with 'Calcein' indicator, under similar conditions, according to the method of Socolar and Salach[2].

Table 2. Comparative summary, ml. of 0·002 *M* Ethylenediamine Tetraacetic Acid/5 mgm. Enamel

Calcium		Magnesium	
Dietary increment of magnesium salts mixture	*Non-salts*	Dietary increment of magnesium salts mixture	*Non-salts*
4·73	4·75	0·22	0·03
4·33	4·60	0·13	0·05
3·65	4·75	0·42	0·19
4·19	4·70	0·49	0·08
4·35	4·42	0·30	0·27
4·13	4·60	0·10	
4·31	4·50	0·28	0·14
3·50		0·30	0·12
Average 4·15	4·61	0·28	0·13

This may be regarded as a first-line, expendable and mobile mineral reserve to save calcium demobilization in the carious process. A more extensive series of further analyses is being carried out in the Chemistry Department, University of Otago, and will support a postgraduate thesis, Dental School, University of Otago.

I am indebted to Prof. W. G. Edwards (now of the Chemistry Department, Royal University of Malta) for his assistance and guidance in the analytical work involved. Thanks are due to Mr. Hughes, Physics Department, University of Otago, for micro-measurements of the depths of enamel surface.

D. B. Ritchie

Department of Chemistry,
University of Otago,
New Zealand.

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Mechanism of Antigen Transformation of Transplantable Rat Tumour

In earlier investigations we have established that in the case of temporary heterotransplantation of Guérin's rat epithelioma to mice, a change occurs in its antigen structure[1]. The change consists in the appearance of an additional antigen, not found in the original tumour. The presence of this antigen could be demonstrated by various methods as late as 5 years after the modification induced by heterotransplantation, although the tumour had been passaged all this time exclusively on rats[2,3].

The question arose as to the mechanism by which this durable modification of the antigen structure of the rat tumour occurs in the course of temporary passaging on mice. The correctness of various hypotheses was tested experimentally and the mechanism of genetic transformation appeared to be most probable. This is shown by the following experiments carried out on the same principle as the classical experiments of Griffith[4] with pneumococci.

A suspension of rat epithelioma cells was prepared and mixed with homogenated mouse lymphocytes. These cells from mouse lymphatic nodes were mechanically disrupted in a glass mortar and suspended in physiological saline in the ratio 1 : 1. This homogenate was mixed with the rat tumour cell suspension in a volume ratio of 1 : 2, 1 : 3 or 1 : 4 and injected subcutaneously to rats.

At the site of injection, inflammation appeared; this subsided after several days and the tumour developed. From such a tumour a new cell suspension was prepared and mixed with the mouse lymphocyte homogenate as before. In this manner a new sub-line of the tumour was obtained which was further passaged on rats in the routine way. The scheme in Fig. 1 shows the branching sub-lines U_I, U_{II}, U_{III} and W_I, W_{II}, W_{III} of the original line of Guérin epithelioma. In successive passages, the antigen structure of the tumour was tested by the method of antibody absorption and complement fixation and referred to the original tumour as well as to the following control antigens: (1) extract of parenchymal organs of normal rats and mice, (2) rat necrotic tissue obtained by intramuscular injection of 0·1 *N* silver nitrate. Several series of these experiments were carried out. In series W_I, W_{II}, W_{III} the Guérin tumour cell suspension was mixed with homogenated lymphocytes of normal *C57BL* mice; in series U_I, U_{II}, U_{III} the lymphocytes of actively immunized mice *C57BL* with Guérin epithelioma were used.

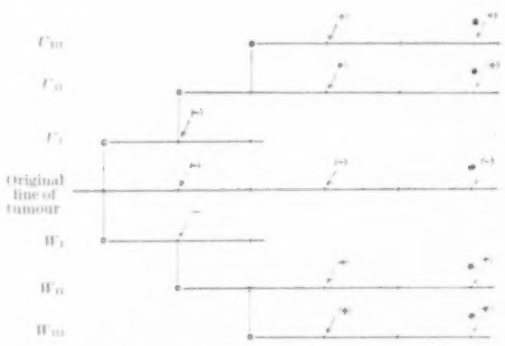

Fig. 1. Scheme of original line and sub-lines of Guérin's epithelioma. Sub-lines W_I, W_{II}, W_{III} produced by mixing the suspension of original Guérin tumour cells with ground lymphocytes of normal mice. In a similar manner the sub-lines U_I, U_{II}, U_{III} were obtained using lymphocytes of mice actively immunized against the Guérin tumour. ⊙, Time of mixing the tumour cells with mouse lymphocytes. The arrows indicate the time of serological examination of the tumours, + and −, presence and absence, respectively, of the additional antigen. Asterisks denote complement fixation tests shown in Table 1. Each section of the line marks a monthly period in which the tumour was passaged

In every phase of the experiment the tumour was examined bacteriologically, and only sterile tumour was taken for antigen structure tests. Such control excludes the possibility of contamination of the Guérin tumour by bacterial antigens.

It was established, as a result of these experiments, that in some rat tumours, under the influence of mouse lymphocyte homogenate, an additional antigen appeared. The latter subsisted in the tumour for 3–4 months in spite of repeated passaging. For illustration a record of one of our serological tests is given (Table 1). No difference was observed between the sub-lines obtained with lymphocytes of normal and immunized mice.

Table 1

Antigens	Dilutions of serum				
	1/16	1/32	1/64	1/128	1/256
T_8, $B_{(1)}$	+ + +	+ + +	+	+	—
T_8, $C_{(1)}$	+ + +	+ + +	+ + +	—	—
T_8, $B_{(2)}$	+ + +	+ + +	+ +	+	—
T_8, $C_{(2)}$	+ + +	+ + +	+ + +	+	—
T_8, C	+ + +	+ + +	+ + +	+	—
T_8 (original tumour)	+ +	+	—	—	—
From mice (C57*BL*)	—	—	—	—	—
From rat	+ +	—	—	—	—
Necrobiotic antigen	+ +	+	—	—	—

Results of complement fixation with specific antiserum $T8C$ adsorbed on original tumour $T8$ particles. This antiserum was used in all experiments as standard. Antiserum $T8C$ was prepared by immunizing rabbits with the sub-line $T8C$ of the Guérin tumour obtained 5 years ago by heterotransplantation on mice (ref. 1).

We believe that in our experiments the disrupted mouse lymphocytes decomposed to smaller particles in the rat organism during inflammation and were possibly incorporated into the genome of the tumour cell.

This enrichment of the tumour cell genome probably brought about the synthesis of an additional cytoplasmic protein manifesting itself as an additional antigen.

The experiments seem to indicate that the mechanism of genetic transformation may be responsible for the antigen modifications occurring in the Guérin tumour. It would be desirable to establish whether a foreign, purified deoxyribonucleic acid molecule will produce a similar transformation. Further experiments in this direction are in progress in our laboratory and the preliminary results seem to confirm this possibility.

In our opinion the mechanism of genetic transformation of somatic cells would be easier to demonstrate if the experiments were performed on anaplastic and poorly differentiated tumour cells and if nucleic acid from normal and highly differentiated cells were used as transforming agent. Under these conditions any property of a highly differentiated cell transmitted to the anaplastic tumour cell can serve as marker.

K. Dux
A. Ryżewska
A. Czarnomska

Department of Tumour Biology,
Institute of Oncology,
Warszawa 22, Poland.

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ANATOMY

Use of Tritiated Thymidine for the Study of the Origin of the Osteoclast

The origin of the osteoclast has been in question for about a century. So far back as 1873, Kölliker[1] maintained that the osteoclast was formed by the fusion of precursor cells and that these precursor cells were osteoblasts. However, Kölliker's work lacked convincing proof, and as a result, numerous theories appeared concerning the origin of the osteoclast. These theories were based largely on morphological studies of metaphyseal osteoclasts. The presence of numerous cell types at this site makes observation of cellular transitions difficult. In order to circumvent this difficulty, we have examined the distal periosteum of young mouse femora, where numerous osteoclasts appear. The cellular complement of the osteogenic layer of the periosteum generally consists of pre-osteoblasts and osteoblasts.

In a previous communication[2], tritiated thymidine was used to label osteoclasts, which were not seen 1 hr. following administration of the isotope (Fig. 1). Numerous osteogenic cells showed uptake of thymidine, but labelled osteoblasts were found less frequently. The actual number of labelled osteoblasts observed was so few that the chance of finding a labelled osteoclast was exceedingly small. In addition, the observations were made 1 hr. following injection of tritiated thymidine. This period of time is too short to allow labelled pre-osteoblasts in DNA synthesis to pass through the post-synthetic and mitotic phases, undergo transformation into osteoblasts, and in turn fuse to form osteoblasts.

The present work has extended the period of observation to 25 days following isotope administration, in order to allow sufficient time for labelled cells to divide, thereby increasing the actual number of labelled periosteal osteoblasts, which increases the chances of demonstrating labelled osteoclasts.

A subcutaneous injection of 0·5 gc. of tritiated thymidine per gm. body-weight was given to 24 four-

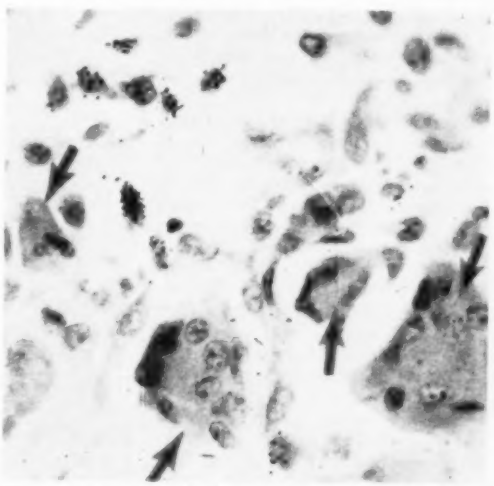

Fig. 1. Autoradiograph of mouse femoral periosteum at the perichondrial region near the distal epiphysis of the femur. Several periosteal cells are labelled with tritiated thymidine 1 hr. after administration of the isotope. The osteoclasts are unlabelled. (Oil immersion, × 470)

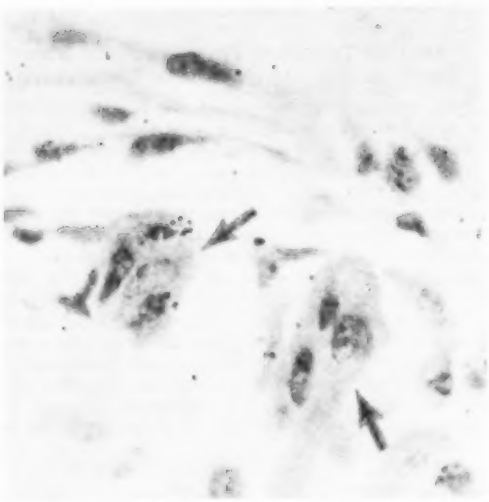

Fig. 2. Autoradiograph of periosteal osteoclasts labelled with tritiated thymidine and observed 36 hr. following the administration of the isotope. (Oil immersion. × 470)

week-old female mice of a *BNL* Swiss albino strain. The animals were killed at various intervals, ranging from 5 min. to 25 days after administration of the isotope. Femora were fixed for 3 hr. in acetic/alcohol (1 : 3) followed by an additional fixation for 24 hr. in formolsaline and 24 hr. of washing. Bone samples were decalcified in a 10 per cent solution of versene. Paraffin blocks were prepared, sections cut at 5μ and autoradiographs prepared with Kodak-*NTB*$_3$ liquid emulsion. Preparations were exposed for 20 days, after which time they were developed and stained with haematoxylin and eosin.

Autoradiographs revealed labelling of periosteal osteogenic cells throughout the entire period. With increasing time following injection of the isotope, additional osteoblasts were seen to be labelled. Labelled osteoclasts were observed for the first time at 36 hr. post injection (Fig. 2). Labelling was seen in one, and less frequently two, nuclei. The remaining nuclear complement was unlabelled. No osteoclastic labelling was observed 10 days following isotope administration.

A previous report[3] has presented direct cytological and cytochemical evidence for the formation of osteoclasts from osteoblasts. It was also shown that osteoclasts do not arise as a consequence of nuclear division, since none was labelled initially. Considering that osteoclasts are being continually renewed, the frequency of labelled osteoclasts depends on the available number of labelled precursor cells as well as other factors. Labelled osteoclasts were not encountered in the present work until an increase in the labelled population of periosteal osteoblasts had occurred. The results show, therefore, that osteoblasts serve as the precursor cells for osteoclasts, and that their polynucleated character arises from the fusion of osteoblasts and not from the repeated division of the osteoclastic nucleus.

This investigation was supported by the U.S. Atomic Energy Commission.

E. A. Tonna
E. P. Cronkite

Division of Experimental Pathology,
Medical Research Center,
Brookhaven National Laboratory,
Upton, New York.

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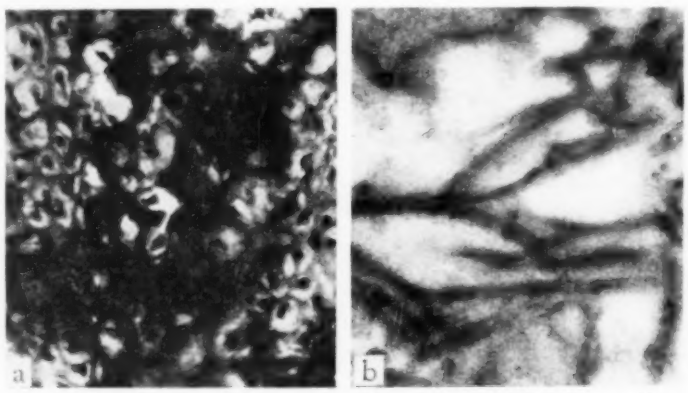

Fig. 1. *a*, Dark areas are heavily calcified, young bone (haematoxylin and eosin. × *c.* 350); *b*, electron micrograph of bony area—note 'seeded' collagen (× c. 36,000)

HISTOLOGY

Influence of Oxygen Concentration and Mechanical Factors on Differentiation of Connective Tissues *in vitro*

Marchand[1] postulated that osteoblasts may differentiate from mesenchymal cells. Recently, it was observed that a strain of cells, derived from adult skeletal muscle, elaborated in tissue culture a substance that appeared to be chondro-osteoid[2]. Since the factors responsible for this cell behaviour were unknown, investigation of the effects of varying mechanical and nutritional factors on a reproducible *in vitro* system of osteogenesis was made. Hanging-drop, Maximov double cover-slip cultures were established from 20-day-old chick embryo tibial cortex and were maintained as described by Fell[3].

Effect of compaction and high oxygen. In one experiment, the cultures were excised periodically from the clot; gassed with a mixture of 35 per cent oxygen, 60 per cent nitrogen and 5 per cent carbon dioxide, and transferred to a new clot. As the cell mass was cut free it usually contracted, thus crowding the increasing population into a more compact state. Cultures were killed on the fourteenth day by fixation in cold 80 per cent alcohol, and serial paraffin sections prepared. Bone was found in 100 per cent of these specimens. In most, a dome-shaped plaque of osseous tissue covered the outer portions. However, in some preparations, where contraction of the culture had been uneven, the bony mass was distorted. The tissue contained numerous young osteocytes, embedded in a

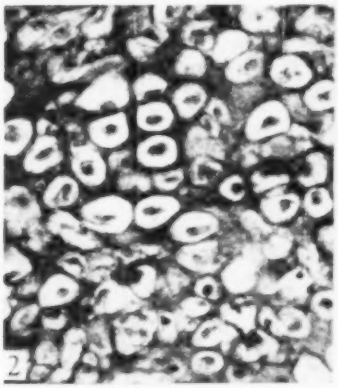

Fig. 2. Dark areas about cells are intensely metachromatic (thionine, × *c.* 350)
Fig. 3. Oriented wavy collagen fibres with interspersed 'fibrocytes' (Van Gieson, × *c.* 487)

matrix which appeared to be predominantly collagenous, when stained by hæmatoxylin and eosin, the van Gieson or Masson trichrome techniques (Fig. 1*a*). When this matrix was stained with thionine, alcian blue or toluidine blue at *p*H 2, 4 and 6, metachromasia was not demonstrable. All osseous areas were heavily calcified, when judged by the reaction with hæmatoxylin, alizarin red *S* and von Kossa stains. Electron-microscopic examination of typical bony areas in these cultures was kindly performed by Dr. James Harkin of the Hospital for Special Surgery and showed collagen fibrils. Many of these fibrils were studded with discrete, electron-dense areas which had an average 640 Å. repeat pattern (nucleation centres or crystal seeds) (Fig. 1*b*). In many aspects, the picture resembled that obtained by Fitton-Jackson[4] in her examination of developing, embryonic chick bone. Very dense areas, believed to be similar to calcification fronts described by Robinson[5], were seen. The deeper portions of these cultures appeared to be cartilage when examined by the light and electron microscope.

Effect of compaction and low oxygen. In a second experiment, the cultures were grown as those just described, except that the oxygen concentration in the gassing mixture was lowered from 35 to 5 per cent, while the nitrogen was raised from 60 to 90 per cent. Under these conditions cells proliferated and migrated well, but no bone was observed. However, hyaline and fibrocartilage were found at the periphery and in all cultures the central areas were less well differentiated. Bundles of collagen, interspersed between relatively small chondrocytes in the fibrocartilage, were stained by the van Gieson technique and deep blue with the Masson trichrome technique. In these areas, no metachromasia was observed. However, in areas having the appearance of hyaline cartilage (Fig. 2), the plumper chondrocytes were surrounded by metachromatic, non-fibrillar matrix. No evidence of calcification was seen in these cultures.

Effect of stretching and high oxygen. In the third experiment, the cultures were prevented from contracting by stretching them over progressively larger silicone rods during the growth period. The other conditions were the same as in the first experiment. No cartilage, bone or calcification was found in cultures that were stretched uniformly. The tissue appeared more like young, growing tendon or fascia. Cells, which resembled mature, elongated fibrocytes, were interspersed between thick, parallel bundles of collagen (Fig. 3). No metachromasia was found in these sections. In some cultures uniform tension in the tissue ring could not be maintained and portions of it contracted. Bony masses with cartilagenous centres were found in the compacted areas, while oriented, fibrous tissue was found immediately adjacent in areas where tension was maintained.

These experiments demonstrate that mechanical (stretching and compacting the cell mass) and nutritional (variations in oxygen) factors, acting in concert, can determine the type of connective tissue that differentiates in a culture of cells arising from bone. Although the mechanisms by which the different tissues were produced are not known, at least two interpretations are possible. First, the conditions in culture may favour one cell-type in a mixed population so that it proliferates and produces a specific extracellular matrix. Second, the conditions in culture may determine the secretory pattern of the cell so that it produces different extracellular matrices in response to different environmental factors. In any event, the results appear to agree with the Maximov concept[6] that certain 'fibroblasts' are pleuripotential and may differentiate in a number of ways to produce the various connective tissues.

This work was supported by grants from the Easter Seal Research Foundation and the Squibb Institute for Medical Research.

C. Andrew L. Bassett
Ingeborg Herrmann

Orthopaedic Research Laboratories,
Columbia University,
College of Physicians and Surgeons,
New York.

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BIOLOGY

Efferent Innervation of Mammalian Muscle-spindles

Mammalian intrafusal muscle fibres are innervated by the small γ-efferent fibres of Leksell[1], which have nerve-trunk diameters of 2–8μ. Fibre size histograms of the intramuscular diameters of both intra- and extra-fusal efferents in fresh and gold chloride preparations show that, while both share the same peak at 3·5μ, about 30 per cent of the intrafusal efferents lie outside the extrafusal range at 4–6μ (ref. 2). These larger fibres have been reported in various descriptions of spindle innervation[3–6]; in cat rectus femoris, they take part in the innervation

of about one-third of the spindles present (Adal and Barker, unpublished). They could be members of either the 2-8α γ-group, or the 8-18α α-group, which have not undergone such extensive branching as the majority of their fellows. The work of Granit, Pompeiano, and Waltman[7] on the α-activation of cat spindles directs attention to the possibility that some members of the α-group may branch so as to innervate both intra- and extrafusal muscle fibres. Such a claim has been made by Weiss and Dutil[8], Cilimbaris[4], Wilkinson[9], Denny-Brown[10], and, more recently, Häggqvist[11]. Wilkinson (echidna spindles) and Häggqvist (monkey spindles) have each published a photograph purporting to show such innervation, but they are unconvincing and open to alternative interpretation. We have examined fifty gold chloride preparations of echidna (*Tachyglossus aculeatus*) spindles without finding instances of collaterals from α-fibres innervating intrafusal muscle fibres, and examination of more than two thousand gold chloride cat spindles, accumulated during work on various aspects of this receptor, has also failed to yield any instance of such innervation. Examination of bat, monkey, opossum, rabbit, and rat spindles has also proved negative in this respect. When apparent examples of such branching have been encountered, closer examination and further tracing has always shown the presence of two discrete fibres; in such instances, the two fibres are usually superimposed one above the other during their course before diverging, so as to give the impression of a single fibre branching into two. Similar instances occur with afferent fibres, and have led to claims[8,12-14] of a single fibre branching so as to terminate in a spindle primary ending and a nearby tendon-organ. If branches of α-efferent fibres do innervate the mammalian spindle, we are of the opinion that the collaterals must originate some distance away from the receptor, either within the muscle nerve or within intramuscular nerve trunks. However, experimental evidence for the innervation of the spindle by α-efferents is conflicting[15], and it seems, on balance, more probable that in mammalian muscle there are discrete intrafusal (γ) and extrafusal (α) efferent systems.

These observations were made during the course of work supported by research grant *B*-1806 from the National Institute of Neurological Diseases and Blindness, U.S. Public Health Service.

D. Barker
N. K. Chin

Department of Zoology,
University of Hong Kong,
Hong Kong.

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Glycogen of *Mactra*

Glycogens, branched chain polymers of glucose containing α-1,4-glycoside bonds in the main chains and α-1,6-glycoside bonds at the branch points, have been identified in the tissues of all animals thus far examined[1]. These polymers are made up of a single kind of sub-unit bonded together by a single type of bond and thus only relatively small differences in the glycogens from different species have been found. The most important difference is in the average chain-length of the molecule, which is inversely related to its degree of branching. This measurement describes quite well the main features of the glycogen molecule, and is therefore of interest to the student of comparative biochemistry. The glycogen of *Mactra* had not been previously characterized; and this communication describes some of the properties of the compound isolated from this pelecypod mollusc.

Specimens of *M. fragilis* obtained from the Supply Department of the Marine Biological Laboratory were used for isolation of glycogen by Pflüger's method: muscle (25·0 gm.) and combined viscera (30·3 gm.) of the animals were digested separately in 50 ml. each of 30 per cent potassium hydroxide on a steam bath. After 30 min. of digestion, homogeneous solutions resulted, and they were cooled and 5 ml. of 0·2 per cent sodium sulphate and 125 ml. of 95 per cent ethanol were added and mixed. The solutions were brought just to the boiling point, and then were chilled and allowed to stand overnight at 3° C. The solutions were centrifuged for 10 min. at 5,000*g* and the resulting supernatant fluid was discarded. The residues were dispersed in 30 ml. distilled water, 1·5 vol. of ethanol were added, and the precipitation was carried out as before. After the muscle glycogen had been precipitated in this way three times and the viscera glycogen four times, the residues were a light tan colour. Following the last precipitation, the glycogen was collected on a sintered glass funnel with gentle suction, and the product was washed on the filter with a little acetone to remove the last traces of a coloured impurity. The resulting white powder was dried *in vacuo* over calcium chloride to constant weight, and was used for the analysis described here.

The ash content of the material was determined by ignition. Samples of the glycogens were hydrolysed in 5 *N* sulphuric acid at 100° C. for 30 min., the solutions were neutralized with dilute sodium hydroxide, and aliquots were taken for reducing sugar analysis and glucose determination by the specific enzymatic reaction with glucose oxidase. The average chain-length was determined exactly as described by Fales[2].

The results of the various analyses are shown in Table 1. In accordance with the experience of other investigators, a significant inorganic residue remains in the glycogen preparations even after repeated alcohol precipitation. The 80 per cent acetic acid precipitation procedure used by Baldwin and Bell for the removal of these salts[3] was not used in the present investigations because of the known lability of the acetal bond in acid. Within the limits of error of the copper reduction method used, all the organic material in the preparations is accounted for as hexose in diglycoside linkage, assuming that these hexoses have a reducing power equivalent to that of glucose. According to the results of the less-precise glucose oxidase analysis, all the hexose is accounted for by glucose itself. Thus the experimental data are con-

the glyceride structure of fats

Jack Sprat, they say, could eat no fat. One can only speculate on the metabolic disorders which led to this curious condition and wonder if our present knowledge could have helped produce something more suited to his digestive system. For we know a great deal now, and much of it is set out in the collective writings of Bailey, Deuel, Hilditch and Lovern. Yet the things we do not know will provide fruitful ground for research for many years to come.

The structure of glycerides alone—basically simple but infinitely variable—is a matter of perennial interest whether one is concerned with natural occurrence, chemical formation, physical behaviour or biological purpose. How significant is the use of a trihydric alcohol? Why are natural fats so specifically constituted? Is it fortuitous or predestined that 1-oleo-distearin and 2-oleo-distearin should have such contrasted physical properties? Do species of natural occurrence represent the limit of useful glycerides? How much can a study of model systems contribute to an understanding of natural products? To what extent does structure influence emulsion systems?

Fats are of prime importance to Unilever, academically—as a means of understanding their role in animal and human nutrition—and commercially for margarine, for cooking and bakery fats, for ice cream. So Chapman, Crossley, Lavery and their colleagues are engaged in a continuing study of all those aspects of structure relevant to their understanding and use.

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ACADEMIC PRESS New York and London

EXPERIMENTAL CELL RESEARCH

Published under the Auspices of the International Society for Cell Biology

Supplement 8

Cell Movement and Cell Contact

Proceedings of the Symposium held by the University of Leiden, at Noordwijk, The Netherlands, September 10–14, 1960

Edited by R. J. C. HARRIS
Imperial Cancer Research Fund, London

May 1961, 281 *pp., illus., cloth bound,* 93*s., paper bound,* 79*s.*

R. J. GOLDACRE. The Role of the Cell Membrane in the Locomotion of *Amoebae*, and the Source of the Motive Force and its Control by Feedback

R. D. ALLEN. A New Theory of Ameboid Movement and Protoplasmic Streaming

E. N. WILLMER. Amoeba-Flagellate Transformation

F. M. CHILD. Some Aspects of the Chemistry of Cilia and Flagella

E. J. AMBROSE. The Movements of Fibrocytes

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sistent with the view that *Mactra* glycogen consists entirely of D-glucose polymerized into chains by glucoside bonds.

Table 1. ANALYSES OF GLYCOGEN FROM *M. fragilis*

	Muscle	Viscera
Yield (gm. per 100 gm. wet tissue)	2·4	2·0
Ash (per cent)	3·1	1·7
Reducing substances (as diglucoside) (per cent)	94·8	96·9
Glucose by glucose oxidase (as diglucoside) (per cent)	108·5	93·3
Average chain-length	15·3	7·3

The result of the average chain-length determination on muscle glycogen is similar to that obtained by Fales[2] with oyster glycogen, and is in the range reported by other investigators who used somewhat different methods of periodate oxidation on glycogen from a variety of species[1-4]. The viscera glycogen of this animal has a considerably shorter average chain-length. The observations do not provide any information about the location in the glucose units of the glycoside bonds, but it may be assumed that they are the customary α-1,4-glycoside bonds with α-1,6-bonds at the branch points.

It is evident that more data on the structure of glycogens from a variety of species must be assembled before any generalizations can be made. Particular emphasis should probably be placed on the examination of material from the most primitive forms available.

These investigations were supported in part by grants from the Association for the Aid to Crippled Children, the Charles A. and Marjorie King Fund, and the National Institutes of Health, U.S. Public Health Service.

DWAIN D. HAGERMAN

Department of Biological Chemistry,
Harvard Medical School,
Research Laboratories of the
Boston Lying-in Hospital,
Boston, Mass., and
Marine Biological Laboratory,
Woods Hole, Mass.

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Absence of Chitinase in *Limnoria*

THE question of the presence or absence of a chitinase in *Limnoria* is of interest for two reasons. First, if a chitinase were present, chitin could serve as a principal nitrogen source. Ray and Julian[1] and Ray[2] have shown that *Limnoria*, which eats wood, can break down cellulose to glucose, and can therefore utilize wood as a source of energy. However, it is not yet known what source of nitrogen *Limnoria* utilizes because wood contains so little. One possible nitrogen source is chitin, present in cell walls of fungi growing in wood and often eaten with the wood[3], and present in the animal's exuviæ, which it may eat.

This question is also of interest for another reason. Since both cellulose and chitin are *B*-glucosides, it is possible that the same enzyme could hydrolyse both; that is, the cellulase found by Ray in *Limnoria* could be a general *B*-glucosidase capable of splitting chitin also.

In an attempt to answer this question, 20, 30, 40 and 60 mgm. of powdered chitin prepared from *Loligo* pens were incubated at 25° and 30° C. for 2–12 days with 0·2 ml. of *Limnoria* enzyme solution and 0·1–0 ml. of McIlvaine's buffer, *p*H 5·6. The enzyme solution was prepared by the method described by Ray[4]. The midgut diverticula of approximately 60 animals were used to make each 0·2 ml. of enzyme solution. At the end of the incubation periods the solutions were tested by paper partition chromatography to determine whether acetylglucosamine or any other reducing sugar had been obtained from the chitin. The tests were all negative, although control solutions of carboxymethyl-cellulose plus enzyme incubated at the same times under the same conditions did contain reducing sugars (mostly glucose) at the end of the incubation periods.

In another experiment, suspensions of chitosan, suspensions of partially hydrolysed chitin, and solutions of carboxymethyl-cellulose were incubated at 30° C. for 7 days with 0·2 ml. of enzyme solution. Each tube contained 20 mgm. of substrate suspended or dissolved in 1 ml. of McIlvaine's buffer at *p*H 5·6. The chitosan was prepared from *Loligo* chitin by treating with hot saturated potassium hydroxide, washing, dissolving in acetic acid, and dialysing against buffer. At the end of the incubation period the solutions were treated as above. No reducing sugar was found, although the control solution of carboxymethyl-cellulose plus enzyme did contain reducing sugar.

Apparently the cellulase present in the midgut diverticula of *Limnoria* is not a general *B*-glucosidase capable of hydrolysing chitin. It is still possible that *Limnoria* produces a chitinase inactive under the conditions tested or that some other portion of the gut produces a chitinase. However, this seems unlikely. Probably, *Limnoria* is not able to utilize chitin as a source of nitrogen.

This work was carried out under contract with the Office of Naval Research[5] and in co-operation with Dr. D. L. Ray.

J. ROSS STEVENSON

Department of Biology,
Kent State University,
Kent, Ohio.

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Comparative Chemistry and the Relationship of the Hamamelidaceae

IN many of the more recent systems of classification, the Hamamelidaceae have been given a central position, several authors believing that they have been derived from rosalian or magnolialian ancestors, and that they, in turn, have given rise to some of the amentiferous families. Although the family is usually included in the Rosales, a number of systematists have assigned it to the order Hamamelidales.

In investigating the relationships of the Hamamelidaceae and those families which have been included in an order Hamamelidales, as well as those of the Rosaceae and some of the amentiferous families, chemical characters have been used.

The chemical characters of the Hamamelidaceae, based on testing twenty-five species representing twelve genera, are the following[1]: (*a*) they are positive to the hydrochloric acid methanol test; (*b*) they are positive to the leuco-anthocyanin test;

(*c*) they give a red reaction to the 'syringin' test ; (*d*) they give a magenta spot with Ehrlich's reagent ; (*e*) they are negative to the hydrogen cyanide test ; (*f*) they are negative to the 'juglone' test ; (*g*) they show no fluorescence in 'juglone' tests ; (*h*) they lack raphides ; (*i*) they lack detectable amounts of glucitol and sedoheptulose ; (*j*) they give the '*Oxalis* reaction' to the cigarette and hot-water tests.

These characters have been compared with those of representatives of the other families tested. Other things being equal, it is assumed that those families which show the closest chemical correspondences are the most closely related.

Of twenty families (Myrothamnaceae, Platanaceae, Cunoniaceae, Eupteleaceae, Stachyuraceae, Eucommiaceae, Cercidiphyllaceae, Trochodendraceae, Buxaceae, Daphniphyllaceae, Coriariaceae, Pittosporaceae, Hydrangeaceae, Saxifragaceae, Bruniaceae, Tetracentraceae, Altingiaceae, Byblidaceae, Podostemaceae and Hydrostachyaceae) which have been included in an order Hamamelidales, representatives of the first fourteen have been tested.

On the basis of results of these tests, one may propose an order Hamamelidales including the Hamamelidaceae, Platanaceae, Myrothamnaceae, and perhaps the Cunoniaceae. This suggestion is based on preliminary work only, but at present there is no chemical evidence against, and much for, such a grouping.

If the sub-family Chrysobalanoideae be excluded, the Rosaceae form a homogeneous group, distinguished by the occurrence of glucitol and cyanogenetic compounds. The chemical evidence indicates that the Rosaceae and the Hamamelidaceae differ sufficiently to make it unlikely that they should be included in the same order ; however, there is no evidence against the view that the Hamamelidaceae are descended from rosalian ancestors.

Representatives of eleven amentiferous families (Garryaceae, Leitneriaceae, Casuarinaceae, Salicaceae, Myricaceae, Juglandaceae, Betulaceae, Fagaceae, Urticaceae, Ulmaceae and Moraceae) have been tested. The chemical evidence indicates that if the Garryaceae, Leitneriaceae and Juglandaceae be excluded, these families form a natural group. There is no evidence against the view that these families have been derived from hamamelidalian ancestors.

E. Shaw*
R. D. Gibbs

McGill University,
Canada.

* Present address: c/o Dept. of Botany, University of Adelaide, Adelaide, South Australia.

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BACTERIOLOGY

Bacterial Polyglycerophosphate

In a previous communication the presence in streptococcal culture supernatants of four serologically distinct red-cell sensitizing antigens was described[1]. One of these antigens, Hickey, which was found to be of wide distribution among the Gram-positive cocci, is almost certainly identical with the non-species specific antigen described by Rantz, Randall and Zuckermann[2]. The distribution of this antigen has been observed to resemble closely that reported by McCarty[3] for a glycerophosphate polymer isolated from various bacterial species, and it seemed possible that we were in fact dealing with the same compound. The polymer as isolated by McCarty had serological properties in that it was precipitated by certain streptococcal antisera—precipitation being inhibited markedly by synthetic polyglycerophosphate prepared by Dr. A. M. Michelson[4]. Glycerophosphate polymers have also been isolated from bacteria by Mitchell and Moyle[5] and by Baddiley *et al.*[6] ; but in neither of these cases were they investigated serologically.

Two samples of synthetic polyglycerophosphate (calcium salts) with average chain-lengths of 6 and 10–15 units respectively have generously been made available by Dr. Michelson, and their capacity to inhibit haemagglutination by the Hickey serum has now been investigated. These tests were carried out with human Group *O* red cells treated for 2 hr. at 37° C. with a digest broth supernatant of the Hickey strain of *Streptococcus pyogenes*. Both compounds had marked haemagglutination-inhibiting capacity—in the test system employed showing appreciable inhibitory activity in a concentration of 30 μgm. per ml. No inhibition of haemagglutination by antisera specific for the other three streptococcal sensitizing antigens described was observed. (These latter tests were carried out with the 6-unit compound). Neither polymer was capable of precipitating with the Hickey antiserum nor of sensitizing red cells to haemagglutination by it. Inhibition was also demonstrated with a mixture of α- and β-glycerophosphates (calcium salts, approx. 45 per cent α-) and with β-glycerophosphate (sodium salt). The inhibitory activity of the latter compounds was, however, relatively slight—that of the α-glycerophosphate mixture being of the order of one-fortieth, and that of β-glycerophosphate one two-hundredth, of that of the polymers.

These results would indicate, therefore, that the serologically active component of the Hickey sensitizing antigen is, like that of McCarty's precipitating antigen, a glycerophosphate polymer the activity of which is probably due to α-glycerophosphate residues. They suggest also the possibility that the serological specificity of other bacterial red-cell sensitizing antigens might also be due to polyol phosphate components.

I wish to express my gratitude to the Medical Research Council of Ireland for financial support.

F. S. Stewart

Department of Bacteriology,
Trinity College,
Dublin.

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Production of Soluble Melanoid Pigments by *Streptomyces* in Gelatin and Glucose Media

During a taxonomic study of several *Streptomyces* cultures, most of which were isolated from soil, experiments were performed on the production of soluble melanoid pigments on two gelatin media—plain 15 per cent gelatin and 15 per cent gelatin plus 2 per cent glucose.

Table 1. Soluble Melanoid Pigment in Media with Gelatin, Glucose and Peptone*

Gelatin	15			15			15			15			15			15			H_2S†
Glucose	—			2			2			—			2			2			
Peptone	—			—			0·5			0·5			—			0·5			
Dist. water	100 S.T.			100 S.T.			100 S.T.			100 S.T.			100 S.S.			100 S.S.			
Days	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	
Strains 511	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
254	+	+	+	—	—	—	—	+	+	+	+	+	+	+	+	+	+	+	+
328	+	+	+	—	—	—	—	—	—	l	+	+	+	+	+	l	+	+	l
399	—	+	+	+	+	+	+	—	—	+	+	+	+	+	+	—	+	+	+
1	l	l	l	—	—	—	—	—	l	l	l	l	l	l	l	l	l	l	—
*B*171	l	l	l	—	l	l	l	l	l	l	l	l	l	l	l	l	l	l	—
64, 135, 361	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

* Sterilization at 16–18 lb. for 20 min., stab culture—spore inoculum. † Difco peptone iron agar. S.T., sterilized together; S.S., sterilized separately. + definitely positive; l, weak; — definitely negative.

Table 2. Soluble Melanoid Pigment in Media with Gelatin and Glucose*

Gelatin	20			20			20			20			20			20			20			20			20		
Glucose	—			0·5			1			2			5			0·5			1			2			5		
Dist. water	100			100 S.T.			100 S.T.			100 S.T.			100 S.T.			100 S.S.			100 S.S.			100 S.S.			100 S.S.		
Days	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30	4	14	30
Strains 511	+	+	—	+	+	+	+	+	+	—	—	+	—	—	+	+	+	+	+	+	+	+	+	+	+	+	+
254	+	+	+	+	+	+	l	l	+	—	—	+	—	—	—	+	+	+	+	+	+	+	+	+	+	+	+
328	+	+	+	+	+	+	+	+	+	—	—	—	—	—	—	+	+	+	+	+	+	l	l	+	l	l	+
399	+	+	—	+	+	+	+	+	+	—	l	+	—	—	—	+	+	+	+	+	+	l	+	—	—	—	—
1	l	l	l	l	l	l	—	l	l	—	—	l	—	—	—	l	l	l	—	l	l	—	l	l	—	—	—
*B*171	l	l	l	l	l	l	l	l	l	—	l	l	—	—	—	l	l	l	l	l	l	l	l	l	l	l	l
64, 135, 361	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

* Sterilization at 16–18 lb. for 20 min., stab culture-spore inoculum. S.T., sterilized together; S.S., sterilized separately: +, definitely positive; l, weak; — definitely negative.

Table 3. Characteristics and Systematic Position of the *Streptomyces* Strains used

Strains	Isolated by	From	Aereal mycelium	Substrate mycelium	Systematic position Kutzner key[1]	Waksman key[2]
(4) 399	Capriotti	Italian soil	Light pink	Cream	II/32	*Strept. zaoeus*
(1) 511	Capriotti	Italian soil	Rose grey	Grey green	—	*Strept.* sp. *A*
(7) 64	Capriotti	Italian soil	Green	Brown	IX/2	*Strept. viridochro*
(8) 135	Capriotti	Italian soil	Grey	Violet	VII	*Strept. violaceus*
(9) 361	Capriotti	Swedish soil	Grey	Greenish	IV/8	*Strept. griseolus*
(2) 254	Capriotti	Italian soil	Green grey	Ochre	IX/4	*Strept. chartreusis*
(3) 328	Capriotti	Swedish soil	Beige	Maroon	VI/23	*Strept. pyridomicetica*
(5) 1	Capriotti	Apple	Grey	Grey	—	*Strept.* sp. *B*
(6) *B*171	Kutzner	German soil	Reddish grey	Colourless to grey	III/1	*Strept. lavendulae*

Strept. sp. *A* and *Strep.* sp. *B* are probably new species.
* It treats of lisogenic strain with all the characteristics of *Streptomyces viridochromogenes* except the production of melanine.
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Three groups of strains could be distinguished: strains with abundant deep-brown pigment on both media, strains with pigment production only on plain gelatin, and strains without pigment production on either medium. Because the production of melanoid pigments plays an important part in *Streptomyces* classification, it was decided to study this phenomenon further. This communication deals with some preliminary experiments on this subject. The experimental results are listed in Tables 1 and 2. (The results in Tables 1 and 2 were obtained in two different experiments and are not strictly comparable because the gelatin concentration was slightly changed.) The presence of peptone (0·5 per cent) in the media had no influence on the production of soluble melanoid pigments.

The effect of glucose on pigment production depends to a certain extent on its concentration and whether it is sterilized together with gelatin or separately. It was found that 0·5 per cent glucose has no effect; 1·0 and 2·0 per cent glucose exhibits a pronounced inhibitory effect on pigment production when sterilized together with the gelatin, but no or only slight inhibition when sterilized separately. 5 per cent glucose inhibits pigment production in all 'positive' strains when sterilized together with gelatin, and in some of them when sterilized separately.

Augusto Capriotti*

Institute of Microbiology,
Rutgers,
The State University,
New Brunswick,
New Jersey.

* Present address: Istituto di Microbiologia Agraria, Perugia, Italy.

VIROLOGY

An Immunizing Antigen from Rabbit-Pox and Vaccinia Viruses

It is well known that infection with vaccinia or one of the other animal pox viruses produces a high degree of immunity, associated with the appearance of neutralizing antibody in the serum. Recently, Collier, McClean and Vallet[1] have shown that neutralizing antibody can also be elicited by vaccinia

virus inactivated by ultra-violet light. But attempts to obtain immunizing material free from virus particles have had little success[2,3]. This communication describes a virus-free immunizing antigen extracted from tissues infected with rabbit-pox or vaccinia viruses. The injection of this soluble material into rabbits resulted in the formation of sera with a neutralizing antibody titre against vaccinia comparable with that found in animals convalescent from rabbit-pox infection.

Rabbit-pox virus (Utrecht strain) was grown for 24 hr. in monolayer cultures of *ERK*1 cells[4]. The infected cells were concentrated to 4×10^7 per ml., and disrupted by ultrasonic vibration. Virus was removed from the suspension by centrifugation and filtration, to give a cell extract which was non-infective when inoculated on to the chorioallantoic membrane of 12-day eggs.

Incubation of the cell extract with a high dilution of hyperimmune rabbit-pox antiserum resulted in disappearance of the neutralizing activity. The substance responsible for this reaction was termed the 'serum-blocking antigen'. A method was developed for the quantitative determination of the serum-blocking activity of a preparation, and this was used to study the properties of the antigen. The serum-blocking antigen was non-dialysable; but it was smaller than the virus, passing a collodion membrane of 330 mμ av. pore diam., and was not sedimented by 20,000*g* for 4 hr. Its titre was reduced about 80 per cent by exposure to trypsin (0·2 per cent crystalline trypsin at 37° and *p*H 8 for 2 hr.), and also by heating (56° at *p*H 7·2 for 1 hr.). It was precipitated by 50 per cent saturated ammonium sulphate, and by dialysis against phosphate citrate buffer *p*H 4·5. At *p*H 7·0, the antigen was adsorbed to *DEAE*-cellulose and was eluted by 0·2 *M* sodium chloride. It also adsorbed to calcium phosphate, being eluted by 0·2 *M* phosphate *p*H 6·7. These findings indicate that the serum-blocking antigen is a protein. Moreover, since the activity was eluted as a single peak from both *DEAE*-cellulose and calcium phosphate columns, it is likely to be a single substance rather than a mixture.

Rabbit-pox virus was also grown in *L* cells, primary rabbit kidney cultures, primary chick embryo cultures, and egg chorioallantoic membranes. The extracts were tested for serum-blocking activity, and all proved to be active. Vaccinia virus was grown in *ERK*1 cells, *L* cells, primary chick embryo cultures, and rabbit skin. Extracts of these tissues also possessed serum-blocking activity.

Having demonstrated a serum-blocking antigen, attempts were made to immunize rabbits. The extract from *ERK*1 cells infected with rabbit-pox virus was injected subcutaneously with adjuvant. The neutralizing antibody response of the animals was measured against vaccinia by Boulter's method[5]. A single injection produced a neutralizing antibody titre of about 1,000 after 4 weeks. Four injections at weekly intervals increased the titre to about 10,000, a level similar to that found in rabbits after recovery from infection with the living virus. The *ERK*1 cell extract was also fractionated on *DEAE*-cellulose, and the individual fractions used to immunize groups of mice. There was good correlation between the ability of fractions to elicit neutralizing antibody and their serum-blocking activity.

The neutralizing antibody formed in response to soluble antigen differed in some ways from that resulting from infection. The slope of the neutralization curve was less steep, with the result that a relatively high concentration of antibody was needed to produce almost complete neutralization of virus. Also, the neutralization titre against rabbit-pox virus was considerably less than that against vaccinia. In view of these differences, it would be unwise to attempt to predict the protective effect of immunization with soluble antigen. This problem is now being investigated.

It is concluded that the growth of rabbit-pox or vaccinia virus in a variety of tissues yields a soluble antigen which both combines with neutralizing antibody and elicits its formation when injected into rabbits or mice. It is hoped that the further study of this antigen will help to elucidate the mechanism of the infection of cells by pox viruses and its neutralization. The protective action of the antigen is not yet known; if effective, it might have practical application in the immunization of patients for whom a living vaccine is undesirable.

G. Appleyard

Microbiological Research Establishment,
Porton, Wilts.

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CYTOLOGY

Chromosome Elimination in Cecidomyidae

Adult members of the gall midges (Cecidomyidae, Diptera) are characterized by possessing a large number of chromosomes in their germ-line cells and a small number in their somatic cells[1]. This difference is established during one or more of the early mitotic divisions when a large but species-specific number of chromosomes is eliminated from all the nuclei destined to form the soma. Elimination is caused by the failure of the majority of the pairs of chromatids to leave the equatorial plate at mitosis.

In *Mayetiola destructor* (Say) there are approximately forty chromosomes in the germ line cells and only eight in the somatic cells of both sexes. Elimination occurs in fourteen nuclei during the fifth mitotic division, when about 80 per cent of the chromosomes are eliminated. The remaining two nuclei, which prior to the fifth mitosis have migrated into the cytoplasm at the posterior end of the egg, do not divide at this time; cell walls surround them to form two pole cells. During subsequent divisions of the pole cells the full number of chromosomes is maintained, and the germ-line is formed.

It has been found that the two nuclei which do not divide during the fifth cleavage become associated at that time with particular granules which lie in the polar cytoplasm, at the extreme posterior end of the egg. Preliminary histochemical investigations indicate that these granules contain ribonucleic acid and are associated with many mitochondria.

In experiments designed to analyse the causes of chromosome elimination the extreme posterior ends

of eggs containing the granulated polar cytoplasm were treated with ultra-violet irradiation before the two nuclei had migrated into this area. The remainder of each egg, containing all the nuclei, was shielded from the irradiation. In such eggs the two posterior nuclei took up their normal position near the polar granules and yet divided with chromosome elimination during the fifth mitosis. Eggs treated in this way later gave rise to embryos with the reduced number of chromosomes in all their cells. The presumptive germ cells, in spite of losing about 80 per cent of their chromosomes, still gave rise to the beginning of a germ line.

Similar effects were obtained by: (*a*) preventing the nuclei from migrating into the polar cytoplasm before elimination by constricting the eggs with fine nylon threads; (*b*) by centrifuging the eggs so that the nuclei were displaced and the polar granules were dispersed throughout the cytoplasm, where the granules lost their apparent function of preventing

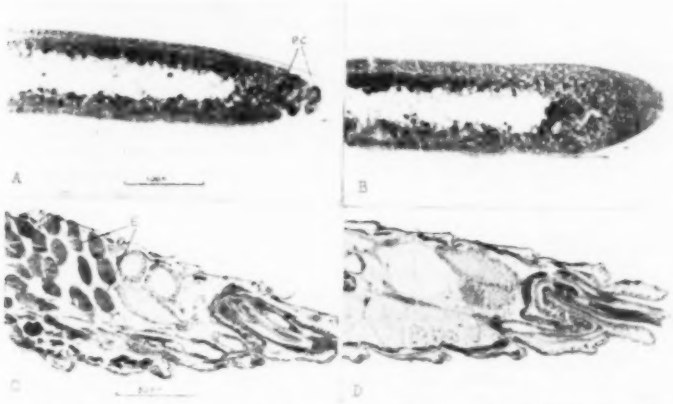

Fig. 1. *A*, Normal embryo at blastoderm stage. The large pole cells (*P.C.*) are at the posterior end; *B*, embryo at blastoderm stage in which the polar cytoplasm had previously been treated with ultra-violet irradiation. Note the absence of large pole cells; *C*, adult female with eggs (*E*); *D*, adult female developed from an embryo treated similarly to *B*. Note the absence of eggs

mitosis. In some eggs of both these experiments division with elimination occurred in all nuclei at the fifth mitosis. The constriction and centrifugation results confirm those of Geyer-Duszynska[2], working on another species.

A few eggs, subjected to the irradiation treatment, were allowed to develop to maturity. So far, only females have emerged and been analysed. It was found that these were sterile and unable to lay eggs, although the secondary sexual characteristics were quite normal. The gonad consisted of a large mass of cytoplasm containing loosely scattered somatic nuclei and degenerating nuclei, apparently belonging to the germ-line. These nuclei were of small size, indicating clearly that they possessed a reduced number of chromosomes.

As a preliminary conclusion it appears that the polar granules prevent chromosome elimination. This might be due to an inhibition of the fifth mitosis in the presumptive germ-line nuclei, or to another mechanism, coinciding in time only with this inhibition. The absence of gametes in pupæ and hatched flies, which had developed from irradiated eggs, indicates that the lost chromosomes are required for gametogenesis.

This work was carried out during the tenure of a Christopher Welch scholarship. I wish to acknowledge advice and encouragement given by Dr. M. Fischberg.

C. Bantock

Embryology Laboratory,
Department of Zoology,
Oxford.

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Synaptinemal Complexes (Cores) in Primary Spermatocytes of Mouse under Elevated Temperature

We have observed in the electron microscope and determined statistically the synaptinemal complexes or cores in primary spermatocytes of male mice, *C57 B1*, exposed to an environment of 34·5° C. and 60 per cent humidity. To avoid confusion from the presence of two generations of spermatocytes in the same section we have evaluated only stages I–VI of the spermatogenic cycle.

According to classical findings, elevated temperature reduces the pairing of homologues[1]. Since our own earlier work[2] and that of others[3–5] has shown that the cores are the chromosomal organelles of pairing, we were interested to observe the effect of elevated temperature on these structures. While the typical complete core is a triplet structure this triplet owes its origin to the coming together of two 'single' structures, one from each homologue; the third structure arises at the line of union[2]. Would elevated temperature result in the presence of the diploid number of unpaired single cores, or would elevated temperature suppress formation of cores proper (triplets)? As shown in Tables 1 and 2 it appears that elevated temperature reduces the total number of cores formed and also interferes with pairing so that the percentage of single cores rises.

A breakdown of the heat-exposed series is given in Table 2.

The time-lag of recovery suggests that the critical biochemical event of core inhibition may occur in the spermatogonia at least 19 days before pairing; but the event can probably also be evoked much more abruptly[6]. Our point of view based on functional and morphological evidence is that the tripartite core, that is, the synaptinemal complex of Moses[3,4] or our core proper, unites two homologous chromosomes in synapsis. This view conforms with those of Fawcett[5], Moses[3,4] Kaufmann[2], and others. In contrast, Sotelo and Trujillo[8] suggest that the tripartite core proper represents a haploid chromosome because they find

Table 1

	Total cells	Total cores	Single cores	Single cores (per cent)	Total cores per cell
Control, 22° C.	69	367	7	2	0·15
Heat-treated, 34·5° C.	56	142	41	29	2·5

Table 2

Treatment	Total cells	Total cores	Single cores	Single cores (per cent)	Total cores per cell
After 28½ hr. heat	10	36	11	30	1·9
After 52½ hr. heat	10	21	8	38	2·1
After 76½ hr. heat, and 14 days recovery	19	60	5	8	3·2
Same, but 19 days recovery	8	25	10	40	3·1

tri-, penta-, and hepta-partite cores in the spermatids of certain insects. While their photographs leave no room for doubt, could not the existence of cores in these insects be a very interesting anomaly? Research on haploid and triploid forms and on strains carrying multiple inversions should settle this point.

The recent work of Charard[9] also agrees with the interpretation of Moses and our interpretation.

This work was performed under the auspices of the U.S. Atomic Energy Commission.

B. R. Nebel
E. M. Hackett

Division of Biological and Medical Research,
Argonne National Laboratory,
Argonne, Illinois.

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GENETICS

Effect of Induced Awn Mutations on Yield in Wheat

From comparisons between sister lines of the same parental derivation segregating in awn character and from experiments using backcrosses, awns have been found to have a positive function as regards grain yield in varieties of bread wheat[1-3]. A spontaneous awned mutant isolated by Mackey[4] in the variety Scandia III outyielded the parent strain in trials carried out over a period of 5 years. Awns have been supposed to influence yield by increasing assimilation and transpiration and thereby the size of the grains. Fully awned mutants frequently occur when varieties belonging to the tipped 1 class of Watkins and Ellerton[5] (that is, awns 1–2 cm. in length and confined to the uppermost spikelets) are treated with both ionizing radiations and chemical mutagens[6]. Several such mutants were found by us in the M_2 progenies of the varieties *N.P.* 799 and *N.P.* 809 treated with phosphorus-32 and sulphur-35 (both 5 μc. per seed), X-rays (16,000 and 22,000 r.) and different dosages of fast and thermal neutrons. Both these varieties have the dominant epistatic gene *B1* on chromosome *5A* (nomenclature of Sears[7]) and the established awn mutations behaved as monogenic changes in genetic studies. The mutants had the somatic chromosome number 42 and no prominent change could be detected in their karyotypes.

Twenty-five awned mutants of *N.P.* 799 and six such mutants of *N.P.* 809 were grown in replicated rod-row trials during 1958. All the awned mutants of *N.P.* 799 yielded more than the parent strain, while in *N.P.* 809 some yielded better and some lower. In both the varieties, the mutants found to be most promising in the first trial maintained their superiority in trials conducted during subsequent years. The yield of these awned mutants is indicated in relation to that of the parents in Tables 1*a* and *b*.

Table 1. Relative Grain Yield of Awned Mutants

(*a*) *N.P.* 799

Trial conducted at :	Awned mutant	Yield (percentage of control) 1958–59	1959–60
New Delhi	799–25	120·11*	109·52*
	799–6	110·00*	103·17
Pusa (Bihar)	799–25	110·85*	104·49
	799–6	102·21	104·24

(*b*) *N.P.* 809

Trial conducted at :	Awned mutant	Yield (percentage of control) 1957–58	1958–59	1959–60
New Delhi	809–1	126·14*	111·12*	102·14
	809–6	106·43*	106·06*	—
	809–9	104·12	—	—
Simla (Himachal Pradesh)	809–6	—	110·68*	—
	809–9	—	106·10	—
Karnal (Panjab)	809–6	—	—	100·86

* Significantly higher.

Of late, there has been much scepticism concerning the possibility of adding through mutation breeding a desirable trait alone to an established variety without simultaneously bringing about some undesirable changes. The agronomic qualities of the fully awned mutants reported in this communication would suggest that in polyploids like bread wheat, which readily withstand whole and part-chromosome deletions, mutation breeding may have considerable scope, particularly if the deletion of a dominant epistatic locus has a favourable effect.

The awned mutants of *N.P.* 799 and *N.P.* 809, the performance of which in yield trials is given in Tables 1*a* and *b*, resembled the parents in all other characteristics like maturity period, shape and quality of grain and rust resistance. Thus the increased yielding ability of some of them could be due to the addition of awns. Vervelde[2] has shown that in warm and dry areas awns play a particularly important part in grain production.

In the plains of India, awned wheats are liked by the farmer since they are damaged less by birds and hence the fully awned mutants of *N.P.* 799 and *N.P.* 809 have a double advantage, that is, they help to satisfy the needs of the farmer and to enhance the yield of the strain. *N.P.* 799–25, an awned mutant which has performed well in the yield trials conducted until now, has been named *N.P.* 836, and it will be tested in larger trials during the coming years.

We are indebted to Drs. B. P. Pal and A. B. Joshi for their advice and encouragement.

D. Jagathesan
C. Bhatia
M. S. Swaminathan

Division of Botany,
Indian Agricultural Research Institute,
New Delhi, 12.

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Transmission of Phosphorus-32 incorporated by Parents into Descendants of *Drosophila melanogaster*

THE quantity and distribution in various phosphorus fractions of phosphorus-32 incorporated into parents by feeding on media containing phosphorus-32 was followed in descendants of *Drosophila melanogaster* strain *Algeria*. The animals were bred at 25° C. in incubators on Belgowsky's culture medium[1] with some drops of a yeast suspension. Reciprocal crosses were made between animals grown on media containing isotopic and normal phosphorus. Repeated passages were carried out in order to eliminate the eventual contamination by phosphorus-32 of the culture media of the descended larvæ by the labelled parents. The fractionation of the phosphorus compounds was carried out according to the Schmit–Tannhauser method[2]. The amount of acid-labile phosphorus in the acid-soluble fraction was assayed by the method of Berenblum[3]. The lipoid-soluble fraction was extracted with a mixture of alcohol/ether (3 : 1). Deoxyribonucleic acid (DNA) was separated after acidification with trichloracetic acid. The protein phosphorus, represented as orthophosphate, was separated from the DNA remaining in the solution by direct phosphorus determination.

The distribution in seven different fractions of phosphorus originating from the culture medium and transmitted to the progeny is shown in Table 1.

Table 1. PHOSPHORUS FRACTIONS IN THE ONTOGENY OF *Drosophila melanogaster* IN γ P/100 LARVÆ

Stage of development	Four-day-old larvæ	Young pupæ	Imagos Female	Imagos Male
Weight per individual (mgm.)	1·82	1·34	1·30	0·92
Fractions :				
Alcohol-soluble	1040	970	1550	380
Acid-soluble	1720	2100	1070	375
Acid-labile	(472)	(1640)	(520)	(54)
Lipoid-soluble	27	23	75	67
DNA fraction	66	102	118	42
Ribonucleic acid fraction	2207	1198	848	532
Protein fraction	111	55	192	333
Total	5171	4448	3853	1729

It may be seen that the intensive morphogenetical processes are preceded by a marked increase in the acid-soluble fraction, mainly at the expense of the alcohol-soluble one. From the pupal stage onwards an increase of lipoid phosphorus was observed. The lowering of ribonucleic acid (RNA) content is significant and might be responsible for the decreasing rate of protein synthesis. A pronounced increase in protein phosphorus was observed in the imago.

Table 2. THE DISTRIBUTION OF PHOSPHORUS ORIGINATING FROM FEMALE AND MALE GAMETES IN THE PHOSPHORUS FRACTIONS OF THE OFFSPRING (γ P/1000 LARVÆ)

Fractions \ Direction of the crosses	Labelled female × normal male	Normal female × labelled male
Alcohol-soluble	4·8	traces
Acid-soluble	8·3	0·130
Acid-labile	(7·4)	(traces)
Lipoid-soluble	1·5	0·042
DNA fraction	1·3	0·054
RNA fraction	6·2	0·099
Protein fraction	3·3	0·150
Total	25·4	0·475

Table 3. THE DISTRIBUTION OF PHOSPHORUS DERIVED FROM THE MEDIUM AND FROM THE GAMETES IN THE F_1 LARVÆ OF *Drosophila* (per cent)

Fractions \ Origin of phosphorus	Culture medium (per cent)	Labelled female gametes (per cent)	Labelled male gametes (per cent)
Alcohol soluble	20·2	18·8	—
Acid soluble	33·4	32·9	27·1
Acid labile	(9·1)	(29·4)	(?)
Lipoid soluble	0·7	5·9	8·7
DNA fraction	1·3	5·1	11·8
RNA fraction	42·2	24·5	20·8
Protein fraction	2·2	12·8	31·6
Total	100·0	100·0	100·0

The distribution of phosphorus-32 in the phosphorus fractions of the larvæ orginating from reciprocal crosses is given in Table 2.

It is clear that the quantity of phosphorus transmitted via the ovocyte is fifty times higher than that transmitted by the male gametes. This figure is probably even higher. We must take into consideration the possibility of polyspermy which is a widespread phenomenon in *Drosophila melanogaster*. In the case of a 25-fold polyspermy the transmission by ovocytes surpasses the male transmission 1,250 times. The possibility that the differences are to be attributed to a higher turnover rate of the ovocytes was eliminated by autoradiographic examinations.

The distribution of phosphorus-32 in the phosphorus fractions derived from the medium, from the gametes or the food is shown in Table 3.

It can be seen that the distribution of phosphorus-32 in various phosphorus fractions derived from food, from male or female gametes, is very different. It is obvious that an equal amount of labelled phosphorus is incorporated into the acid-soluble compounds of the alcohol-soluble fraction from both the food and the ovocytes. By contrast, only traces of a similar incorporation were found if the transmission took place via the male germ-cells. There was no remarkable difference in the acid-soluble fraction; however, more phosphorus was incorporated into the acid-labile fraction via the ovocytes than from the food. Relatively less phosphorus was recovered in DNA if incorporated directly from the food than after transmission via the gametes. The differences between the phosphorus content of the RNA and protein fractions might be explained by the different amounts of reserve substances and cytoplasm contained by the ovocytes.

B. FALUDI
I. CSUKÁS
K. SZÉPLAKY
F. Á. DÁNIEL

Department of Phylogenetics and Genetics,
Eötvös Loránd University, Budapest.

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Hexaploid *Dactylis*

A RECENT intensive survey of *Dactylis* has shown that tetraploids ($2n = 28$) are widely distributed throughout the temperate parts of the world[1]. In Europe and Asia, regions where this genus is native, diploids are also found, and each of these has a comparatively limited range of distribution[2].

Table 1. Meiotic Pairing

Plant No.		Metaphase I pairing: I	II	III	IV	V	VI	VII	X	Mean chiasmata	Total pollen mother cells
Be 4556 4	Mean	0·32	9·31	0·96	5·76	0·36	1·0	0·20	0·04	34·28	25
	Range	0–1	7–17	0–2	0–3	0–2	0–4	0–1	0–1		
Be 4556 13	Mean		17·30		1·00		0·40	—	—	34·05	20
	Range	—	16–21		0–4		0–2	—	—		
Be 4556 14	Mean	—	11·40	0·40	3·00	—	1·0	—	—	34·40	5
	Range	—	6–15	0–2	3		1–3				

As a result of screening 175 populations derived from Europe, Western Asia, the Mediterranean and North Africa, wild hexaploids have been discovered in material from Cyrenaica, and these have been compared with wild hexaploids from Egypt, sent to us by Mr. R. Knight, of the Waite Agricultural Research Institute[1].

Taxonomically, these plants are indistinguishable from forms of *Dactylis glomerata* ssp. *hispanica* Domin. Both groups as grown at Aberystwyth have a stout root-stock with bulbous-based tillers, slender, stiff, tough leaves with markedly toothed margins, and slender wiry culms up to 60 cm. tall. The heads are usually compact, the range of forms which occur being similar in both groups. The florets are short, the lemmas having pubescent keels and the lobed apex characteristic of ssp. *hispanica*[4].

The first introduction formed part of a collection made by the Food and Agriculture Organization[5], and originated from the top of Tocra Pass, Cyrenaica, at an altitude of 350–400 m., with a yearly rainfall of about 300 mm. The soil was a stony red clay-loam (Accession No. *Be* 4556 = F.A.O. 3076). The second population was collected at Rasel Hekma, at a low altitude in the Western Desert of Egypt, with a rainfall of 100 mm. (Accession No. *Be* 4860).

Chromosome counts were made at meiosis on four plants from Tocra Pass[6]. Twelve of the Rasel Hekma plants were counted at Adelaide, and five of their progeny at Aberystwyth. All were hexaploid. Meiotic behaviour (Fig. 1) was studied by Keith Jones in 50 pollen mother cells of three Cyrenaica plants; the results are given in Table 1, showing some variation in pairing from plant to plant. In plant 13, bivalents predominated, quadrivalents and hexavalents were few and no odd number associations were seen. On the other hand, plant 4 is an interchange heterozygote, and partly as a consequence of this, multivalents were more frequently observed.

It seems probable that, in population plants not heterozygous for interchanges, bivalent pairing will be the general rule. Forty per cent of the cells in plant 13 formed bivalents only.

The size and fertility of the hexaploid pollen was assessed (Table 2). The fertility equals that found for diploid and tetraploid *Dactylis*[7]. The diameter of the pollen of the hexaploid was less than that generally

Table 2. Pollen Data

Ploidy	Material	Pollen: Diameter (arbitrary units) Mean	Range	Fertility (per cent)
2×	8 populations, including 7 sub-species	7·88	7·13–8·72	78
4×	6 populations, including 3 sub-species	9·09	8·67–9·60	82
6×	1 genotype, a twin seedling from a tetraploid	8·55	—	84
	Be 4860, 1 population	8·40	8·00–9·10	88
	Be 4556, 1 population	—	—	83

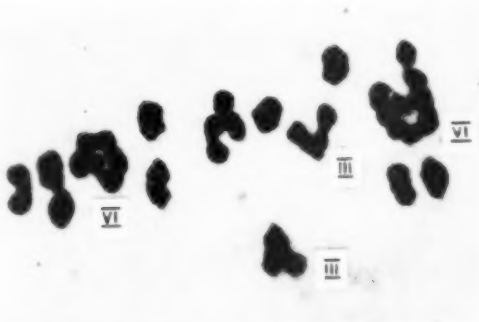

Fig. 1. *Be* 4556, No. 4. 2*n* = 42. 2 VI, 2 III, 12 II

found in the tetraploids, and we consider that this is probably associated with the extreme xeromorphic adaptation of these plants.

The discovery of hexaploid *Dactylis* in two localities in the same geographical area suggests that the type may have a much wider distribution in this region. Ecologically, these forms are adapted to dry conditions in areas of low average rainfall, and long periods of summer drought. These plants may, of course, grow in sites favoured by extra run-off moisture, as described by Boyko[8] for a *Dactylis* ecotype in Israel, which we found to be tetraploid (Accession No. *Be* 4160). Even so, unequal distribution rather than actual amount of annual rainfall is probably the critical factor in relation to tolerance of drought.

The two most probable modes of origin of the hexaploid are by somatic doubling in a triploid hybrid, or following the occurrence of non-reduction in a tetraploid. Wild triploids have been reported from Israel in areas where diploids and tetraploids meet[9]. We suppose that the hexaploids arose by the doubling of such triploids, which, if they possessed favourable new combinations of genes, might be adapted to survive in the most extreme habitats, and be able to colonize such areas in the event of the chance restoration of fertility by chromosome doubling.

Martin Borrill
Keith Jones*

Welsh Plant Breeding Station,
Plas Gogerddan, Aberystwyth.

* Present address: Royal Botanic Gardens, Kew.

[1] Borrill, M., *J. Linn. Soc. (Bot.)*, **56**, 368, 441 (1961).
[2] Stebbins, G. L., and Zohary, D., *Univ. Calif. Pub. Bot.*, **31**, No. 1, 1 (1959).
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[4] Domin, K., *Acta Bot. Bohem.*, **14**, 3 (1943).
[5] List of Grassland Ecotypes collected by F.A.O. in 1954 and 1955 in *The Natural Vegetation of the Mediterranean Region and the Near East*, p. 11.
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[7] Borrill, M., *Genetica* (in the press).
[8] Boyko, H., and Tadmor, N., *Bull. Res. Council Israel*, **4**, 241 (1954).
[9] Zohary, D., and Nur, Y., *Evolution*, **13**, 311 (1959).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, May 1

INSTITUTION OF ELECTRICAL ENGINEERS, ELECTRONICS AND COMMUNICATIONS SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. R. Graham, Mr. J. W. H. Justice and Mr. J. K. Oxenham: "Progress Report on the Development of a Photo-electric Beam Index Colour Television Tube and System".

SOCIETY OF ENGINEERS (at the Engineering, Marine, Welding and Nuclear Energy Exhibition, Olympia, London), at 5.30 p.m.—Mr. R. H. Bound: "Jet Propulsion for Boats".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Dr. Tom A. Margerison: "The Presentation of Science". (First of three Cantor Lectures on "The Presentation of Science and the Arts on Television".)

SOCIETY OF CHEMICAL INDUSTRY, LONDON SECTION (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Annual General Meeting, followed by Mr. E. G. Peppiatt: "Chemistry in the Service of a New Industry".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Capt. R. H. Grant, M.C., R.M.: "The Conquest of Annapurna II".

Monday, May 1—Tuesday, May 2

ELECTRICAL ASSOCIATION FOR WOMEN (in London)—Thirty-sixth Annual Conference.

Tuesday, May 2

INSTITUTION OF ELECTRICAL ENGINEERS, MEASUREMENT AND ELECTRONICS SECTIONS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. D. W. Pashley: "Structural Properties and Applications of Evaporated Metal Films"; Mr. J. R. Balmer: "Deposition of Evaporated Non-magnetic Films".

Wednesday, May 3

ZOOLOGICAL SOCIETY OF LONDON (in the Meeting Room, Zoological Gardens, Regent's Park, London, N.W.1), at 10 a.m.—Symposium on "Biological Acoustics".

BRITISH INSTITUTION OF RADIO ENGINEERS, COMPUTER AND RADAR GROUPS (at University College, Gower Street, London, W.C.1), at 3 p.m.—Symposium on "Computer Control of Air Traffic".

INSTITUTE OF PHYSICS and the PHYSICAL SOCIETY (in the Physics Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7), at 5 p.m.—Dr. Scott E. Forbush (Carnegie Institution of Washington): "The Equatorial Electro-Jet in Peru".

INSTITUTE OF PETROLEUM (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Mr. W. K. B. Marshall and Mr. V. L. Holmes: "Recent Developments in Arc Welding as Applied by the Petroleum Industry".

SOCIETY FOR ANALYTICAL CHEMISTRY (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Scientific Papers.

Wednesday, May 3—Thursday, May 4

INSTITUTIONS OF CIVIL, MECHANICAL, AND ELECTRICAL ENGINEERS (at the Institution of Civil Engineers, Great George Street, Westminster, London, S.W.1)—Railway Modernization Conference.

IRON AND STEEL INSTITUTE and the INSTITUTE OF METALS (at the Hoare Memorial Hall, Church House, Great Smith Street, London, S.W.1), at 2.30 p.m. on Wednesday and 10 a.m. on Thursday—Symposium on "Structural Processes in Creep".

IRON AND STEEL INSTITUTE (at the Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, London, S.W.1)—Annual General Meeting.

Thursday, May 4

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. D. M. S. Bagguley, Mr. R. A. Stradling and Mr. J. S. S. Whiting: "Cyclotron Resonance Over a Wide Temperature Range. 1: Germanium. 2: Silicon".

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. J. W. L. Beament, Dr. H. E. Hinton, F.R.S., Dr. S. M. Manton, F.R.S., and Dr. John Smart: "On Aspects of the Classification of Insects".

INSTITUTE OF REFRIGERATION (at the Institute of Marine Engineers, The Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Mr. G. P. Smedley: "Metals for Refrigeration and Other Low Temperature Installations".

UNIVERSITY COLLEGE, LONDON (in the Chemistry Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. J. Hamilton: "Advances in Elementary Particle Physics".*

UNIVERSITY OF LONDON (at the Senate House, University of London, Malet Street, London, W.C.1), at 5.30 p.m.—Prof. Roger Y. Stanier (University of California): "Bacterial Photosynthesis".*

CHEMICAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Prof. A. J. Birch, F.R.S.: "Some Pathways in Biosynthesis" (Simonsen Lecture).

Friday, May 5

INSTITUTION OF THE RUBBER INDUSTRY and the PLASTICS INSTITUTE (at the Institution of Electrical Engineers, Savoy Place, London, W.C.2), at 9.30 a.m.—Conference on "Foamed Rubber and Plastics".

INSTITUTION OF ELECTRICAL ENGINEERS, MEDICAL ELECTRONICS DISCUSSION GROUP (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Artificial Muscles" opened by Dr. A. B. Kinnear Wilson.

ROYAL AERONAUTICAL SOCIETY (at 4 Hamilton Place, London, W.1), at 6 p.m.—Mr. R. Hafner: "The Helicopter—The First of the VTOL Aircraft".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. Bart J. Bok (Canberra): "The Southern Milky Way".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER or ASSISTANT LECTURER IN THE DEPARTMENT OF PHILOSOPHY—The Registrar, The University, Leeds 2 (May 6).

LECTURER (preferably with an interest in physical biochemistry or the study of enzymes and their mechanisms) IN BIOCHEMISTRY—The Registrar, Manchester College of Science and Technology, Manchester 1 (May 6).

RESEARCH ASSISTANT (chemist, preferably with two or three years research experience) for work on volatile inorganic compounds, in collaboration with Dr. L. H. Long—The Secretary, The University, Exeter (May 8).

LECTURER IN PHARMACOLOGY—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (May 9).

LECTURER IN THE DEPARTMENT OF LOGIC AND METAPHYSICS—The Secretary, The University, Edinburgh (May 10).

LECTURER or ASSISTANT LECTURER IN THE DEPARTMENT OF INORGANIC AND STRUCTURAL CHEMISTRY—The Registrar, The University, Leeds 2 (May 12).

SENIOR LECTURER IN PHARMACY in the Science Department, Jamaica College of Arts, Science and Technology, Kingston—Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (May 12).

ASSISTANTS (2) IN CIVIL ENGINEERING—The Secretary of University Court, The University, Glasgow (May 13).

RESEARCH FELLOW IN PURE MATHEMATICS—The Registrar, University College, Singleton Park, Swansea (May 13).

SENIOR SCIENTIFIC OFFICER SCIENTIFIC OFFICER PHYSICISTS (with a first- or second-class honours degree in physics, chemistry or metallurgy or equivalent) at the National Physical Laboratory, Teddington, Middlesex for (1) development of fine gratings and detectors for X-rays in the wave-length region 1 Å. to 100 Å. and (2) application of diffraction gratings to the precise measurement of X-ray wavelengths—The Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1 (quoting A.162/A (May 13).

ASSISTANT IN THE DEPARTMENT OF MORAL PHILOSOPHY—The Secretary, The University, Edinburgh (May 15).

LECTURER IN AGRICULTURAL CHEMISTRY, with special reference to Animal Biochemistry and Nutrition—The Secretary, Wye College (University of London), near Ashford, Kent (May 15).

LECTURER or ASSISTANT LECTURER (preferably with an interest in the fields of mycology and plant pathology) IN THE DEPARTMENT OF BOTANY—The Assistant Registrar (Science), The University, Edgbaston, Birmingham 15 (May 15).

LECTURERS and ASSISTANTS IN EXPERIMENTAL PHYSICS, THEORETICAL PHYSICS AND ELECTRONICS—The Secretary, The University, Aberdeen (May 15).

LECTURER IN CHEMICAL ENGINEERING—The Registrar, University College, Singleton Park, Swansea (May 20).

LECTURER (with a degree in veterinary science from an approved university, or equivalent, and at least three years postgraduate experience, including small animal practice) IN VETERINARY MEDICINE at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 20).

ORGANIC CHEMIST (with a university degree or technical college diploma in organic chemistry, or equivalent qualifications, and preferably experience with biological systems) IN THE DIVISION OF PLANT INDUSTRY, C.S.I.R.O., Canberra, A.C.T., Australia, to collaborate with a research group investigating the chemical nature and mechanism of action of growth regulators isolated from plants—Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 130/469 (May 20).

LECTURER (preferably with a special interest in geomorphology) IN GEOGRAPHY—The Registrar (Room 22, O.R.B.), The University, Reading (May 27).

DEMONSTRATOR (zoologist, botanist or geneticist) IN BIOLOGY—The Registrar, The University of Adelaide, Adelaide, South Australia (May 29).

READER IN CHEMICAL METALLURGY at the Imperial College of Science and Technology—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 29).

SENIOR LECTURERS (2) (one with special interests in the field of mycology, and the other in anatomy, ferns or algae) IN THE DEPARTMENT OF BOTANY, University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (May 30).

RESEARCH FELLOWS (2) IN THE DEPARTMENT OF ANTHROPOLOGY AND SOCIOLOGY, Institute of Advanced Studies, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, May 31).

SENIOR LECTURER or LECTURER (with postgraduate experience in research, coupled with a keen interest in teaching) IN PHYSICS at the University of Hong Kong—The Secretary, Association of Universities

of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, May 31).

LECTURER IN PHILOSOPHY at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia and London, June 1).

READER (with appropriate academic qualifications and teaching experience) IN PHILOSOPHY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, June 9).

BIOCHEMIST (honours graduate), to assist with research on lipid metabolism in gastric mucosa—Dr. Billing, Department of Medicine, Royal Free Hospital, London, W.C.1.

BIOMETRICIAN (graduate with mathematical and biological interests, and preferably a knowledge of statistics) IN THE SECTION OF STATISTICS, for duties involving consultation and research on design and analysis of experiments—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, Berks, quoting Ref. 61/12.

CHIEF TECHNICIAN (Grade I) IN THE DEPARTMENT OF ZOOLOGY, to take charge of the technical staff and services of the Department, and to assist with planning in connexion with a proposed new building—The Assistant Bursar, The University, Reading.

INFORMATION OFFICER (university graduate with at least three years information experience, preferably in science and technology, and the ability to supervise professional staff)—The Director, Ashb, 3 Belgrave Square, London, S.W.1.

LECTURER (graduate in physics or chemical engineering) IN PHYSICS—The Principal, National College of Food Technology, St. George's Avenue, Weybridge, Surrey.

LECTURER IN BIOLOGY IN THE TRAINING DEPARTMENT, with particular interest in natural history—The Warden, University of London, Goldsmiths' College, New Cross, London, S.E.14.

LECTURER (with qualifications in applied chemistry or chemical engineering, and experience in industry, research or teaching) IN THE DEPARTMENT OF CHEMICAL TECHNOLOGY—The Secretary, Royal College of Science and Technology, George Street, Glasgow, C.1.

LECTURER (with research experience) IN CHEMISTRY, to teach undergraduates and carry on fundamental research—Prof. J. K. S. Jones, Queen's University, Kingston, Ontario, Canada.

PHYSIOLOGIST OR ZOOLOGIST (recent graduate) IN THE PHYSIOLOGY DEPARTMENT, to assist with research on the bio-assay of hormones in blood—The Secretary, National Institute for Research in Dairying, Shinfield, Berks, quoting Ref. 61/11.

RESEARCH ASSISTANTS (2) (with a Ph.D. or suitable taxonomic experience) IN PLANT TAXONOMY, to collaborate in compiling a flora of Turkey—Dr. P. H. Davis, University Department, Royal Botanic Gardens, Edinburgh 3.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Henry Wiggin and Co., Ltd. Publication No. 1941: Machining Wiggin High-Nickel Alloys. (London and Birmingham: Henry Wiggin and Co., Ltd., 1959.) [271

The Organization and Financing of Research in Biochemistry and Allied Sciences in Great Britain. Edited by K. S. Dodgson. Pp. 51. (London: The Biochemical Society, 1960.) 2*s.* 6*d.* [301

National Museum of Wales. Fifty-third Annual Report, 1959–60. Pp. 78 + 4 plates. (Cardiff: National Museum of Wales, 1960.) [301

Sabouraudia, Vol. 1, Part 1 (January 1961). (Journal of the International Society for Human and Animal Mycology.) Pp. 72 + 12 plates. Subscription price per volume (four issues) 80*s.*; or 12 dollars. Single parts 20*s.*, or 3 dollars. (Edinburgh and London: E. and S. Livingstone, Ltd., 1961.) [301

Regional Advisory Council for Technological Education—London and Home Counties. Twelfth Annual Report, 1959–60. Pp. 48. (London: Regional Advisory Council for Technological Education—London and Home Counties, 1961.) [301

Department of Agriculture and Fisheries for Scotland. Spaced-Plant Trials at East Craigs. VII: Varieties of Cocksfoot *Dactylis glomerata* L., 1956–58. Pp. 6. (Edinburgh: Department of Agriculture and Fisheries for Scotland, 1961.) [301

Ministry of Agriculture, Fisheries and Food. Bulletin No. 154: Grassland Management. Third edition. Pp. v + 69. (London: H.M. Stationery Office, 1960.) 4*s.* 6*d.* net. [311

Empire Cotton Growing Corporation. Progress Reports from Experiment Stations, Season 1959–60. Republic of the Sudan. Pp. 33. 2*s.* 6*d.* Uganda. Pp. 45. 2*s.* 6*d.* (London: Empire Cotton Growing Corporation, 1960.) [311

Ciba (A.R.L.), Ltd. Technical Notes, No. 217 (January, 1961): "Tecton" Roofing Units. Pp. 6. (Duxford: Ciba (A.R.L.), Ltd., 1961.) [311

Problems of Cybernetics, 1. Chief Editor: A. A. Lyapunov. Translation Editor: Richard Goodman. Consulting Editor: A. D. Booth. Translated from the Russian by M. Nadler, F. J. Griffiths, G. Kiss and S. A. Muit. Pp. 1–214. (London and New York: Pergamon Press, 1960.) 210*s.*; 30 dollars. [311

Scottish Education Department. Technical Education in Scotland: The Pattern for the Future. Pp. 16. (Cmnd. 1245.) (London: H.M. Stationery Office, 1961.) 1*s.* net. [22

Ministry of Agriculture, Fisheries and Food. Agricultural Chemical Approval Scheme (Insecticides, Fungicides and Herbicides): List of Approved Products, 1961. Pp. 93. (London: Ministry of Agriculture, Fisheries and Food, 1961.) [22

Science Masters' Association and the Association of Women Science Teachers. Science and Education: a Policy Statement issued by the Science Masters' Association and the Association of Women Science Teachers. Pp. 12. 1*s.* net. Chemistry for Grammar Schools. Pp. 39. 2*s.* net. Biology for Grammar Schools. Pp. 24. 2*s.* net. Physics for Grammar Schools. Pp. 39. 2*s.* net. (Sections of Part I of the Science and Education Report issued by the Science Masters' Association and the Association of Women Science Teachers, to be read in conjunction with the Policy Statement.) (London: John Murray (Publishers), Ltd., 1961.) [22

Department of Scientific and Industrial Research: Warren Spring Laboratory. Mineral Processing Information Notes. No. 1: Supercritical Grinding—a Survey of Current Research. Pp. ii + 15. No. 2: Cyclones in Mineral Processing—a Review of Current Information. Pp. iii + 29. (London: Department of Scientific and Industrial Research, 1960.) [22

Field Studies Council. Annual Report, 1959–60. Pp. 32 + 4 plates. (London: Field Studies Council, 9 Devereux Court, W.C.2, 1961.) [32

Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences. No. 703, Vol. 243 (2 February, 1961): The Terminations of the Afferent Nerve Fibre in the Muscle Spindle of the Frog. By B. Katz. Pp. 221–240 + plates 26–61. 60*s.* No. 704, Vol. 243 (2 February, 1961): The Organization of the Atrial Nervous System of Amphioxis (*Branchiostoma lanceolatum* (Pallas)). By Q. Bone. Pp. 241–269 + plates 62–65. 16*s.* (London: Royal Society, 1961.) [32

Discovery Reports, Vol. XXXI, pp. 1–222 + plates 1–3: Swimbladder Structure of Deep-Sea Fishes in Relation to Their Systematics and Biology. By N. B. Marshall. 55*s.* net. Vol. XXXI, pp. 123–208: The Benguela Current. By T. John Hart and Ronald I. Currie. 75*s.* net. (Cambridge: At the University Press, 1960.) [32

Other Countries

Tanganyika. Records of the Geological Survey of Tanganyika, Vol. 8, 1959. Pp. ii + 113 + 18 plates. Shs. 17.50. Geological Survey of Tanganyika. Memoir No. 11: The Rungwe Volcanics at the Northern End of Lake Nyasa. By D. A. Harkin. Pp. ix + 172 + 31 plates. Shs. 25. (Dar-es-Salaam: Government Printer, 1960.) [271

United States Department of the Interior: Geological Survey. Water-Supply Paper 1524: Quality of Surface Waters for Irrigation, Western United States, 1957. Prepared under the direction of S. J. Love. Pp. viii + 183 + plate 1. (Washington, D.C.: Government Printing Office, 1960.) 1 dollar. [271

Annual Report of the Board of Regents of the Smithsonian Institution showing the Operations, Expenditures, and Condition of the Institution for the year ended June 30, 1959. Pp. x + 693 + 92 plates. (Publication 4392.) (Washington, D.C.: Government Printing Office, 1960.) [271

Astronomical Photographs—Prints—Slides—Transparencies from the collection of the Yerkes Observatory. 1960 edition. Pp. 36. (Chicago: Yerkes Observatory, University of Chicago, 1960.) [301

Food and Agriculture Organization of the United Nations. FAO Agricultural Studies, No. 51: Vibrio Fetus Infection of Cattle. Edited by J. A. Laing. Pp. iv + 62. (Rome: Food and Agriculture Organization of the United Nations; London: H.M. Stationery Office, 1960.) 5*s.*; 1 dollar. [301

Smithsonian Institution. Annual Report of the United States National Museum for the year ended June 30, 1960. Pp. vi + 175. (Washington, D.C.: Government Printing Office, 1960.) [301

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Applications are invited from suitably qualified persons for appointment to the above position. The appointee, who will be responsible to the Physicist-in-Charge, will be required to assist in the general administration of the Physics Department and take an active part in research. Through the Peter MacCallum Clinic, the Board provides a Radiotherapy service for a population of approximately three million in the States of Victoria and Tasmania and carries out specialized research in this field. In addition to conventional X-ray therapy equipment, one 4 MeV linear accelerator is in operation in Melbourne and the installation of a second will commence shortly. A theratron junior (Cobalt-60) unit is in use in Launceston, Tasmania. The responsibilities of the Physics Department include the provision of a medical physics service to clinical and special departments, the radiation protection of personnel and the conduct of research into problems associated with the work of the Institute. There are excellent laboratories and technical workshop facilities are available. Qualifications: Applicants should have a degree in physics and should state their experience in medical physics and electronics. Salary: Salary will be according to qualifications and experience up to a maximum of £A 2,750 per annum. Other conditions of appointment include sick, long service and recreational leave. Superannuation equivalent to the F.S.S.U. scheme is available. Substantial assistance will be given for the payment of fares and removal expenses.

Full conditions of appointment may be obtained from the undersigned, with whom applications, stating age, qualifications and experience, and including the names of at least two referees, close on June 2, 1961.

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These posts offer good opportunities for promotion within the Research Department of the Generating Board.

Forms of application may be obtained from the Assistant Regional Secretary (Personnel), Central Electricity Generating Board, North-Eastern and Yorkshire Region, 1 Whitehall Road, Leeds, 1, to whom they should be returned to arrive not later than May 12, 1961.

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Applications are invited for Senior Lectureship in Crop Husbandry from graduates in botany, agriculture or horticulture, with teaching and research experience at university level. Knowledge of tropical crops highly desirable, but not essential. Duties include leading the teaching and research programme of the Crop Production section. Salary scale £1,500 by £75 to £2,425 per annum, plus £250 per annum local allowance (pensionable). Entry point determined by qualifications and experience. Child allowance, F.S.S.U. Unfurnished accommodation, if available, at rental of 10 per cent of basic salary. Up to five full passages on appointment, normal termination and triennial study leave.

Detailed applications (six copies), naming three referees, as soon as possible to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

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(No. 130/479)

The appointee will be required to work in a collaborative programme in developmental biophysical chemistry. Applicants with experience in synthetic organic chemistry and in one of the following physico-chemical fields: co-ordination chemistry, electrochemistry or surface chemistry will be preferred. An interest in the relationships between molecular structure, physico-chemical properties and biological activity would be an advantage.

Applicants should be Honours graduates in Chemistry (or equivalent qualifications) with some years relevant postgraduate research experience.

Salary: Dependent on qualifications and experience within the range £A 1,510 to £A 2,265 per annum.

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(No. 130/480)

The appointee will collaborate with the Division's expanding group working on the chemistry and biology of antifungal substances. He will be required to carry out research on the structure and synthesis of naturally occurring antifungal compounds and their analogues.

Applicants should be Honours graduates in Organic Chemistry (or equivalent qualifications) with post-graduate research experience in structural or synthetic Organic Chemistry.

Salary: Dependent on qualifications and experience within the ranges: £A 1,510 to £A 2,265 or £A 2,395 to £A 2,720 per annum.

Salary for a female will be £A 180 per annum less than corresponding rates for men.

Both positions are offered for an initial period of three years.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

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Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting relevant Appointment number) should be addressed by May 27, 1961.

BRADFORD INSTITUTE OF TECHNOLOGY

DEPARTMENT OF BIOLOGICAL SCIENCES

Applications are invited for the post of Senior Lecturer in Microbiology. Candidates should be qualified to teach microbiology to final degree and Diploma in Technology standard. Salary scale in accordance with the Burnham Technical Award, namely, £1,550 to £1,750 per annum. The successful candidate will be encouraged to develop industrial contacts and to undertake research for which adequate facilities are available. Previous industrial and research experience, at a suitable level, will be taken into account in fixing the commencing salary.

Further particulars and forms of application may be obtained from the Registrar (Department F), Bradford Institute of Technology, Bradford, 7.

HENRY PATTEN,
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Applications are invited from research workers with specialized knowledge and experience in animal research for appointment in the grade of Senior Principal Scientific Officer. The salary scale attaching to the appointment will be £2,650 by £100 to £2,750 by £125 to £3,000 per annum, and the superannuation arrangements will be those afforded by the F.S.S.U.

Further particulars may be obtained from the Secretary of the Organization at 48 Palmerston Place, Edinburgh, 12, to whom applications, accompanied by the names and addresses of three referees, must be submitted not later than May 31, 1961.

ROWETT RESEARCH INSTITUTE

Applications are invited for the Headship of the Pig Section of the Applied Nutrition Department. The post is superannuated and will be in the Senior Scientific or Principal Scientific Officer grade, according to experience and age. A good honours degree in science or its equivalent and previous research experience essential. A rented house is available. Salary scales (Provincial): Senior Scientific Officer, £1,302 to £1,604; Principal Scientific Officer, £1,666 to £2,368.

Applications, stating date of birth, with particulars of education and experience, together with the names of three referees, should be sent to the Secretary, Rowett Research Institute, Bucksburn, Aberdeen.

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Write in confidence to: Mr. K. M., Box No. 1470 Amman, Jordan.

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Detailed applications (six copies), naming three referees, as soon as possible to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

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Further particulars should be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on June 1, 1961.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY
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DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY

The Governing Body invite applications for three posts, Senior Lecturer, Lecturer and Assistant (Grade B) in Physiology and in Pharmacology. Honours Degree essential. Duties include teaching and research. The salary scales attached to these grades are as follows: (a) Senior Lecturer, £1,550 by £50 to £1,750; (b) Lecturer, £1,370 by £35 to £1,510 by £40 to £1,550; (c) Assistant (Grade B), £700 by £27 10s. to £1,150, plus additions for training and graduate status. There is, in addition, a London allowance of £38 or £51, according to age. Successful applicants will be placed on these scales in accordance with previous experience and/or industrial experience.

Particulars and form of application from the Clerk to the Governors. Applications to be submitted by May 20, 1961.

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The post calls for a man who desirably—but not essentially—has a veterinary qualification. He should, in any case, be experienced in helminthology and anthelmintics. A knowledge of helminth immunity would be an advantage. Preferred age range 24 to 30.

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Applications, in duplicate and giving the information listed in the final paragraph of the general conditions of appointment, should reach the Registrar, The University of Adelaide, Adelaide, South Australia, not later than June 15, 1961.

LINCOLN COUNTY HOSPITAL

Non-medical Biochemist (basic grade) required. Salary maximum £1,150 per annum. Vacancy in the Lincoln Area Biochemistry Laboratory.

Applications, with the names and addresses of two referees, not later than May 22, 1961, addressed to Group Secretary, County Hospital, Lincoln. Candidates need not necessarily have hospital experience. Scientists expecting graduation this year will be considered. Further details obtainable from Pathologist.

RESEARCH FELLOWSHIPS (3 YEARS) in Government Scientific Establishments: Value £1,325 to £1,640 per annum (Senior) and £910 to £1,220 per annum (Junior). A very wide range of topics in physics, mathematics, chemistry, engineering, biology and other fields. Qualifications: normally first- or second-class honours degree; evidence of high standard of ability in research; and at least two years' postgraduate research experience (three years for Senior Fellowships). Those completing these periods of experience in 1961 may apply. F.S.S.U.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form, quoting **S/5244/61.**

UNIVERSITY OF LONDON
READERSHIP IN CHEMICAL METALLURGY AT IMPERIAL COLLEGE

The Senate invite applications for the Readership in Chemical Metallurgy tenable at the Imperial College of Science and Technology (salary scale £1,675 to £1,975 to £2,425 a year, plus £80 London allowance).

Applications (10 copies) must be received not later than May 29, 1961, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF CAPE TOWN
CHAIR OF BOTANY

Applications are invited for the Harry Bolus Chair of Botany. The occupant of this Chair will be Head of the Department of Botany. The salary scale is R.4,600 by R.200 to R.5,400 per annum (£2,300 by £100 to £2,700 per annum).

Applicants should state their age, experience and qualifications, and give details of research work published or in progress. They should also give the names of at least two referees, whom the University may consult. Two copies of the application and testimonials should reach the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (from whom memoranda giving the general conditions of service (including transport expenses on appointment) and information on the work of the Department should be obtained) not later than May 20, 1961. An additional copy should be sent direct by airmail to the Registrar, University of Cape Town, Private Bag, Rondebosch, Cape Town, South Africa, to reach him by the same date. Applicants should state the date on which they could assume duty if appointed. The University reserves the right to appoint a person other than one of the applicants or to make no appointment.

UNIVERSITY OF LONDON
GOLDSMITHS' COLLEGE TRAINING DEPARTMENT

Applications are invited for the post of Lecturer in Biology in the Training Department with particular interest in Natural History. Good teaching experience in Schools essential. Salary on Pelham Scale for Lecturers in Training Colleges.

Applications (five copies) to the Warden, University of London, Goldsmiths' College, New Cross, London, S.E.14, from whom further particulars can be obtained.

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(2) Mechanical Engineer with bias for one or more of: (i) hydraulically operated mechanisms, including servo-control; (ii) mechanics of machines (theory and practice); (iii) hydro- (or aero-) dynamics of fairly elementary character.

(3) Hydrodynamicist (or aeronautical engineer), with some years' experience for work on torpedo dynamics.

(4) Mechanical Engineers (servo-mechanisms, gyro design and develop). Electrical Engineers (Electronics/Design). Mathematicians (Operational research and theoretical physics). Physicist (acoustics).

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Qualifications for all posts first- or second-class honours degree or equivalent in appropriate subject. Must normally be natural born British subjects of natural born British parents. Senior Scientific Officers must have had minimum three years' postgraduate experience and be not less than 26 years of age.

Salaries: (A.) Senior Scientific Officer, £1,302 to £1,604; Scientific Officer, £717 to £1,186. (B., C., D.) Senior Scientific Officer, £1,342 to £1,654; Scientific Officer, £738 to £1,222.

Appointments unestablished (with F.S.S.U. benefits) but opportunities for those between 21 and 32 to compete for established posts.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference and post.

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Applications are invited for Assistant Lectureships in the College from graduates in (a) Chemistry or Biochemistry, (b) Microbiology, (c) Physics or Engineering. Facilities for research are available. Salary scale: £790 by fifteen at £27 10s. and one at £37 10s. to £1,240 per annum. Starting salaries dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

UNIVERSITY COLLEGE
IBADAN, NIGERIA

Applications are invited for two posts of Senior Lecturer in Department of Botany. One appointee should have special interests in field of Mycology, the other in Anatomy, Ferns or Algae. Appointments to commence October, 1961. Salary scale £2,275 by £75 to £2,575 per annum. Passages paid for appointee, wife and up to five children under 11 years, on appointment, annual overseas leave and termination. F.S.S.U. Children's, car and outfit allowances. Part-furnished accommodation at rent not exceeding 7.7 per cent of salary.

Detailed applications (six copies), naming three referees, by May 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

SCHOOL OF AGRICULTURE
KUMASI COLLEGE OF TECHNOLOGY, GHANA

Applications are invited for the following posts: (a) Lectureship in Agricultural Chemistry; (b) Lectureship in Entomology. Applicants for post (a) should have a good honours degree in Chemistry or Agricultural Chemistry with teaching and/or research experience and a definite bias for Organic Chemistry and Biochemistry. Applicants for post (b) should hold a good honours degree in Entomology or Zoology, with research or teaching experience. Postgraduate experience in a crop protection or a pest control establishment would also be a most useful qualification. The successful candidates will be required to teach students working for a four-year Diploma Course in Tropical Agriculture and will be expected to conduct research in their respective subjects. The School has available about 600 acres of land which is being developed as an experimental farm and research station, where investigations in a large range of problems are being conducted.

The Ghana Government intends to establish Kumasi College of Technology as an autonomous University in the very near future, and teaching then may be up to General Degree level. Contract appointments are normally for five years, and may be renewed. Three months' notice of resignation of an appointment is required on either side. The contract salary scale is £1,110 by £60 to £1,950 per annum. Candidates with wide experience may be appointed at Senior Lecturer level. In addition, children's allowances are paid up to a maximum of three, and a gratuity at the end of the contract at the rate of £150 for each year of satisfactory service. The entry point is fixed according to qualifications and experience. This salary scale is, however, under review. The College is fully residential, and members of staff are housed in pleasant modern bungalows on the spacious campus; climate and living conditions are good. Annual leave with three free return passages in four years is granted to members of staff and their families.

Application forms and an Information Brochure may be obtained from the Assistant Registrar, Kumasi College of Technology, 29 Tavistock Square, London, W.C.1, who will also be glad to answer any questions about these appointments.

TEA RESEARCH INSTITUTE OF EAST AFRICA
P.O. BOX 91, KERICHO, KENYA COLONY
AGRICULTURAL CHEMIST

Applications are invited for the post of Chemist. The duties of this post are: responsibility for a routine soil-testing laboratory; conducting research on tea soils and on the nutrition of the tea bush. Applicants should possess a degree in Chemistry from an approved University, together with at least two years' postgraduate experience. A working knowledge of experimental statistics is essential. Salary is in the scale £1,225 by £75 to £1,750 per annum; entry point according to qualifications and experience. Free quarters with heavy furniture, or an equivalent allowance. There is a contributory Pension Scheme. Overseas leave, six months every three years or three months every two years, subject to the exigencies of the Institute's work; three weeks' local leave a year. Free passages by sea or tourist air are provided on appointment and on overseas leave for self, wife and children under fifteen years. The Institute's research station is situated in a healthy district of the Kenya Highlands, seven miles from the flourishing township of Kericho, centre of the largest tea-growing area of East Africa. Kericho has a Government European Primary School, Anglican and Roman Catholic Churches, and good shopping facilities. Further details relating to local conditions (e.g., income tax, etc.) will be supplied on request.

Applications, giving the names of two professional and one personal referee, should be sent by airmail to the Director, to arrive not later than June 1, 1961.

SOUTH MANCHESTER H.M.C., GROUP Laboratory, Withington Hospital, Manchester, 20. Applications are invited for the post of Assistant Biochemist. Candidates should preferably possess a first- or second-class honours degree, Associateship or Graduate Membership of the Royal Institute of Chemistry. The initial salary is in the range of £650 to £730 per annum. (Basic grade Whitley Council scales.) The post provides excellent opportunities for experience in hospital biochemistry, and the Biochemistry Department has recently been modernized and fully equipped.—Applications, with the names of two referees, should be sent to the Group Pathologist, Withington Hospital, Manchester, 20, as soon as possible. 3063.

RESEARCH IN FIBRES AND PLASTICS

FORMICA LIMITED

Research and Development Department

Formica Limited is a member of De La Rue—a rapidly expanding international group of companies with a reputation for leadership in a number of specialized fields.

The research department has a strength of 70 people, and is at present located in Tynemouth, Northumberland. It is planned to increase this number to at least double over the next few years, during which the department will move to a new research building in the South of England.

A major part of the present and proposed activities of Formica Limited is inseparably bound to the use of synthetic and natural fibres in combination with polymeric materials.

Applications are invited from

PHYSICAL CHEMISTS, PHYSICISTS or CHEMICAL ENGINEERS

for research in the field of

Fibres and Fibre Resin Systems

Only those with an excellent academic record and a genuine enthusiasm for research in this field will be considered.

The person chosen will join a new research group now being formed, and there are excellent prospects of rapid promotion to Research Leader.

He will receive a commencing salary of up to £2,000 per annum, dependent upon his previous record.

Correspondence, which will be treated in confidence, should be addressed to:

The Research Director,
FORMICA LIMITED,
West Chirton, North Shields, Northumberland.

Formica Limited—a subsidiary of the De La Rue Company Ltd.

UNITED KINGDOM ATOMIC ENERGY AUTHORITY

require

EXPERIMENTAL STAFF

to join teams at Aldermaston studying a wide variety of theoretical and mathematical problems arising in the field of nuclear energy, including hydrodynamics (partial differential equations) and neutronics (Boltzman transport equations). The I.B.M. 7090 computer is used for the numerical study of these problems.

Applicants should have a pass degree, H.N.C. or equivalent qualification. Experience in one of the above fields would be an advantage.

Salary: £640 to £2,005, according to age, qualifications and experience.

Superannuation scheme. A house or substantial assistance with house purchase will become available for married officers living beyond daily travelling distance.

Please write for application form to the Senior Recruitment Officer, A.W.R.E., Aldermaston, Berks, quoting ref. 2938/34.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY
ASSISTANT LECTURER IN CHEMICAL ENGINEERING

Applications are invited from chemical engineers, physicists, chemists or mechanical engineers, or from mathematicians having experience in applied science. If the person appointed does not have the Ph.D. he can work for this. Salary in scale £800 by £50 to £950, plus £60 per annum London allowance, family allowances and F.S.S.U. membership.

Further particulars from Professor K. C. Denbigh, Department of Chemical Engineering and Chemical Technology, Imperial College of Science and Technology, London, S.W.7, to whom applications should be sent by May 15.

VETERINARY OFFICERS, RESEARCH Officers, Assistant Veterinary Investigation Officers: Ministry of Agriculture, Fisheries and Food. Pensionable posts for men and women aged at least 23. M.R.C.V.S. normally required, and postgraduate experience desirable. Present vacancies for Research Officers in virology, bacteriology and biochemistry. National salary scales £926 (at 23) to £1,269 (at 32 or over) rising to £1,420, then to £1,778. Promotion prospects.—Write Civil Service Commission, Burlington Gardens, London, W.1, for application form, quoting 130-173-265/61. Early application advised.

COMMONWEALTH OF AUSTRALIA

DEPARTMENT OF DEFENCE

STAFF REQUIRED
FOR

ADVANCED EDP SYSTEMS

DESIGN, DEVELOPMENT AND APPLICATION.

An EDP Proving and Training Centre is to be set up in the Australian Department of Defence at Canberra, A.C.T., to introduce large-scale, integrated EDP systems of advanced design into the Navy, Army and Air Force. This Centre is to develop and prove these systems in sequence commencing with that for the Air Force, and is to train staff for their effective operation.

A number of vacancies exist in this Centre and the Services organisations for experienced staff of various specialisations in the following fields:

EDP Systems Analysis, Design and Development.
Programming and Programme Development for Large Digital Computer Configurations.
Data Transmission and EDP Reporting Techniques.
Operations Research using Digital Computers.
Advanced Techniques of Scientific Management and Numerical Analysis.
Supervision and Control of Large Digital Computer Systems.
Supervision and Control of EDP Data Collection and Preparation Staff and Equipment.

Appointments will normally be made within the following classifications, although suitable outstanding applicants may be offered higher classifications:

SENIOR PROGRAMMER

GRADE 2 (£A2,655–2,980) and GRADE 1 (£A2,525–2,720)

At least three years' practical EDP system experience with specialised knowledge and qualifications in one or more of the above fields required.

PROGRAMMERS

GRADE 2 (£A2,265–2,460) and GRADE 1 (£A1,840–2,070)

At least one year of practical EDP system experience with specialised knowledge and qualifications in one of the above fields required.

SENIOR EDP OPERATOR (£A1,563–1,665)

At least three years' practical experience in supervising and scheduling the operation of a large-scale digital computer system, or in supervising and controlling specialist data collection and preparation staff, required. Computer programming and coding experience desirable.

On entering into an agreement to remain with the Department of Defence for three years, first-class travel to Canberra will be provided for a successful applicant and his wife and children. A reasonable amount of household goods will also be transported to Canberra where housing or other suitable accommodation will be made available.

Applications, with supporting personal and professional resumés, should be sent to the following address by May 15, 1961. Selected applicants will be interviewed during June, 1961.

The Official Secretary, Australia House, The Strand, London, W.C.2.

SHELL

"SHELL" RESEARCH LIMITED

require a

RESEARCH ASSISTANT

for the

CHEMISTRY DIVISION

at their Tunstall Laboratory, Broad Oak Road, Sittingbourne, Kent

The work of the Chemistry Division includes the formulation of chemicals for biological evaluation; the design and operation of inhalation chambers; and the development of micro-analytical techniques for the determination of biologically active compounds in tissues, body fluids and the atmosphere. The Laboratory has an extensive programme of work covering a very diverse range of compounds.

Applications are invited from candidates with Higher National Certificate in chemistry or equivalent, and some 5 to 10 years' laboratory experience; experience in instrumental techniques of analysis would be an advantage.

Salary will be based entirely on qualifications and experience. Five-day week, staff restaurant, attractive Pension Scheme, bus service to door. Applications in writing to:

The Personnel Superintendent, (Reference TL/RA/DC), "Shell" Research Ltd., Woodstock Agricultural Research Centre, Near Sittingbourne, Kent.

UNITED NATIONS

The International Atomic Energy Agency seeks highly-qualified experts for Technical Assistance appointments in the following fields:—

Agricultural applications of radioisotopes:
(1) Korea—12 months.
(2) Morocco—6 months.
(3) Pakistan—12 months.

Analysis of nuclear raw materials:
(1) Indonesia—6 months.
(2) Sudan—6 months.

Applications of radioisotopes in animal husbandry:
Argentina—3 to 6 months.

Health physics: Philippines—6 months.

High temperature ceramics: Argentina—6 months.

Irradiation techniques: Philippines—6 months.

Material-testing by irradiation: Tunisia—12 months.

Medical applications of radioisotopes:
(1) Brazil—6 months.
(2) Philippines—6 months.

Medical physics: Guatemala—3 months.

Neutron physics: Greece—12 months.

Nuclear electronic equipment:
(1) Ceylon—6 (possibly 12) months.
(2) Mexico—6 months.
(3) Pakistan—4 months.

Nuclear physics: Turkey—12 months.

Prospecting for nuclear raw materials: Mexico—6 months.

Radiation dosimetry: Mexico—3 months.

Radiobiology: Indonesia—12 months.

Radiochemistry:
(1) Brazil—12 months.
(2) Indonesia—12 months.

Toxicology of radioactive materials: Yugoslavia—3 months.

Uranium chemical concentrates production: Mexico—3 months.

Uranium metal or oxide production:
(1) Argentina—9 months.
(2) Mexico—6 months.

Salaries range between £217 and £298 per month, plus generous allowances; all emoluments are tax-free. For job descriptions and application forms write urgently to Ministry of Labour, 26 King Street, London, S.W.1, quoting E9/AEA/5, and stating post(s) applied for.

UNIVERSITY OF LONDON COMPUTER UNIT

Applications are invited for the following posts:

Lecturer, on the scale £1,050 by £50 to £1,400 by £75 to £1,850, plus £60 London allowance, to take part in the teaching, advisory and research activities of the Unit. Research Fellow, in the range £1,000 to £1,300, mainly to develop research in new computer applications. The appointment will be for two years. Special consideration will be given to candidates with experience in numerical analysis/information processing.

Applications, with details of qualifications, experience, and names of two referees, to be sent to the Director, University of London Computer Unit, 44 Gordon Square, W.C.1, not later than May 22.

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Research Fellow in Chemical Crystallography in the Department of Chemistry in the Faculty of Science to undertake investigations into the structures of complex natural products of biological importance and novel structural interest. Excellent facilities are available for single crystal analysis and electronic computation. The Fellowship, valued at £875 per annum, will be available for one year from October 1, 1961, in the first instance, but renewal may be possible. Applicants should have had training in single crystal analysis and should possess a Ph.D. degree or have had at least three years' postgraduate experience.

Applications should be received not later than May 31, 1961, by the Registrar, University of Manchester, Manchester, 13, from whom further particulars and forms of application may be obtained.

DIRECTOR OF RESEARCH BANANA BOARD, JAMAICA

Applications are invited for the post of Director of Research by the Banana Board, a statutory body. The Director will be expected to take charge of the Board's Research Department, which has been in operation for six years, and to direct the research programme comprehending all aspects of the banana industry from field to ship, including the control of diseases in field and storage.

Appointment will be on contract with salary according to qualifications and experience, but at a minimum of £3,000 per annum, plus appropriate allowances, leave passages, etc.

Applications should be submitted to the Secretary, Banana Board, P.O. Box 602, Kingston, Jamaica, W.I.

WORLD HEALTH ORGANIZATION

invites applications, which should be made within two weeks of the date of issue of this advertisement, for a post of

QUALIFIED CHEMIST

DUTIES: To serve as chemist for a research team in LAGOS (Nigeria) evaluating the performance of residual insecticides under field conditions. Experience in the analyses of chlorinated hydrocarbon and organophosphorus insecticides and the determination of cholinesterase levels in human blood essential. Should be capable of setting up laboratory facilities to meet the project requirements, prepare reports and recommendations on findings and suggestions on methods, techniques and procedures and of training and teaching other chemists or laboratory assistants.

REQUIREMENTS: Degree of Master or Doctor of Science in chemistry or in chemical engineering, preferably with major in analytical chemistry. At least three years' experience in the field of chemistry and physical chemistry. Good fundamental knowledge of biology and biochemistry. Good knowledge of English and working knowledge of French essential.

SALARY: $U.S.6,000 per annum, net of income tax, rising by annual increments to $8,000 plus cost of living, assignment and dependants' allowances and education grant for children under certain conditions. Thirty working days annual leave each year with paid home travel every two years. Initial two-year contract with one year probationary period.

Detailed curriculum vitae should be sent to Chief, Personnel, W.H.O., Palais des Nations, Geneva, marking the outside of the envelope "VN 643". Further information and application forms will be sent only to those candidates who seem suitable for serious consideration.

UNIVERSITY OF CAMBRIDGE
SCHOOL OF VETERINARY MEDICINE

Graduate Research Assistant required to work in group studying respiratory diseases. Post-graduate experience with tissue-culture methods or infective disease research would be an advantage. Veterinary qualification not essential.

For particulars apply to the Administrative Secretary, School of Veterinary Medicine, Madingley Road, Cambridge.

United Kingdom Atomic Energy Authority

TWO ASSISTANT MANAGERS

are required by

THE RADIOCHEMICAL CENTRE, AMERSHAM

POST 1 (Ref. 34/2/61). An experienced **PHYSICIST** is required to take charge of two teams within the Physics Department which are working on nucleonic instrumentation and the highly accurate measurement of radioactivity.

Applicants must have a good honours degree in physics and have had considerable experience in several of the following fields:

The design of electronic equipment involving pulse circuitry or of nucleonic measuring equipment; dosimetry of ionising radiation; measurement of radioactivity; elucidation of nuclear decay schemes; the use of radioisotopes in industry or research.

POST 2 (Ref. 34/4/61). **A CHEMIST, ENGINEER or PHYSICIST** is required to take charge of a group which develops and manufactures sealed sources of alpha, beta and gamma radiation for clinical, industrial and scientific uses.

Applicants must have a good honours degree or equivalent. They must have had substantial relevant industrial or research experience which should include handling radioactive materials.

The appointments will be in the grade of Principal Scientific Officer and starting salaries will be based on experience within the range £1,840 to £2,590.

Both posts are superannuable and financial assistance may be given towards the purchase of a house.

Apply to the Personnel Officer, the Radiochemical Centre, Amersham, Bucks, quoting the appropriate reference.

UNIVERSITY OF SHEFFIELD

Applications are invited for the W. J. Rees Research Fellowship tenable in the Department of Refractories Technology in the Faculty of Metallurgy. The object of the Fellowship is to advance knowledge in the field of Refractory Materials; candidates should already have some research experience, but not necessarily in this field. Normal tenure will be five years, but the appointment will be for two years in the first instance and thereafter will be renewable annually. The starting salary will normally be £1,000 a year with annual increments of £50 and F.S.S.U. provision. A higher salary may be paid to a successful candidate with outstanding qualifications and experience.

Applications (three copies), including the names and addresses of referees and, if desired, copies of testimonials, should reach the Registrar (from whom further particulars may be obtained) not later than May 29, 1961.

UNIVERSITY OF AUCKLAND
NEW ZEALAND
SENIOR LECTURESHIP OR LECTURESHIP IN ELECTRICAL ENGINEERING

Applications are invited for the above-mentioned post. Candidates should be University graduates in Electrical Engineering; a higher degree would be an advantage. Previous lecturing experience is not essential. The salary scale for a Senior Lecturer is £1,750 per annum rising to £2,000, and for a Lecturer £1,250 rising to £1,700 per annum. Commencing salary within the appropriate scale will be determined according to qualifications and experience. An allowance will be made towards travelling expenses.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in New Zealand and London, on June 15, 1961.

UNIVERSITY OF BIRMINGHAM
DEPARTMENT OF CHEMICAL ENGINEERING

Applications are invited for the post of Lecturer (£1,050 by £50 to £1,400 by £75 to £1,550; £1,550 by £75 to £1,850); Assistant Lecturer (£850 by £50 to £950) in Chemical Engineering. The initial stipend will be related to qualifications and experience. A knowledge of either petroleum production engineering or of colloid or surface phenomena desirable but not essential. The post, tenable from October 1, 1961, carries F.S.S.U. and family allowance benefits.

Applications (three copies), naming three referees, should be sent by May 31, 1961, to the Assistant Registrar (Science), The University, Edgbaston, Birmingham, 15, from whom further particulars may be obtained.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

The Chemistry Department has two vacancies:—Ref. 61/14: Experimental Officer required to take part in research on ruminant nutrition and milk composition, and to be responsible for analytical work, including gas chromatography and other modern techniques. Candidates should have suitable analytical experience. Ref. 61/15: Assistant Experimental Officer required to assist in studies of mineral metabolism in cattle. Candidates should be interested in both chemical analysis and working with animals. Candidates should be graduates or hold A.R.I.C., H.N.C., or an equivalent qualification, or for the Assistant Experimental Officer post G.C.E. "A" level or an equivalent if under 22. Salary scales: 61/14, £1,057 to £1,336; 61/15, £450 10s. to £983. A contributory pension scheme is in operation.

Application forms from the Secretary, N.I.R.D., Shinfield, Reading, quoting appropriate ref. no.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

ORGANIC CHEMISTS

(TWO POSITIONS)

The Organization's Division of Organic Chemistry, Chemical Research Laboratories, Fishermens Bend, Melbourne, Victoria, invites applications for two positions (one at senior level) of Organic Chemist to participate in their current programme of investigations aimed at the isolation and structure determination of biologically-active substances, of natural origin. The Division's research in this field embraces studies of materials from plants, insects and micro-organisms.

Applicants should be Honours graduates majoring in Chemistry (or hold equivalent qualifications). Experience in research on natural products is essential and an interest in biological problems and some experience of handling biological material will be an advantage.

Salary: Dependent on qualifications and experience within the ranges: £A.2,395 to £A.2,720 per annum or £A.2,980 to £A.3,500 per annum, or within the ranges: for senior level £A.1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the range within which the original appointment is made.

Fares paid. Further particulars supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 606/25) should be addressed by June 1, 1961.

MSL *have been retained to advise on this appointment.*

PERSONAL ASSISTANT

and potential general manager for a dairy company employing about 1,000 in processing, bottling, wholesaling and retailing in the Midlands.

He will understudy one of the directors and will assist in developing an additional profit unit with its own processing dairy and fleet of vehicles.

Candidates must have a public school education followed by commercial and management experience in the dairy industry or in a company processing and selling foodstuffs.

Preferred age 28 to 32 years. Initial salary £1,750 with car, non-contributory pension and life insurance. Please send brief details in confidence quoting reference U.2644 to J. G. Smith

MANAGEMENT SELECTION LIMITED
17 Stratton Street, London, W.1

In no circumstances will a candidate's identity be disclosed to our client unless he gives permission after a confidential interview at which he will be given full details of the appointment.

INSPECTOR OF MINES

NORTHERN RHODESIA

Qualifications: Diploma or degree in Mining of recognized School of Mines or University. At least five years' experience, preferably in metalliferous mining industry, including knowledge of underground ventilation practice.

Age Limits: 25 to 45.

Duties: Enforcement of mining and explosives legislation, inspection of mines and accident investigation.

Terms of Appointment: On agreement for one tour (36 months) with prospect of permanent appointment after a probationary period. Emoluments in the scale £1,065 to £2,095. Free passages, quarters at rental, free medical attention, generous leave, taxation at local rates.

Apply to Director of Recruitment, Colonial Office, London, S.W.1, briefly stating age, qualifications and experience and quoting BCD.99/3/06/C1.

SCHOOL OF PHARMACY

KUMASI COLLEGE OF TECHNOLOGY, GHANA

Applications are invited for the following posts: (a) Lecturer in Pharmaceutical Chemistry; (b) Lecturer in Pharmacognosy. Applicants for post (a) should hold a degree in Chemistry or Pharmacy; for post (b) a degree in either Botany or Pharmacy. In both cases the applicant should be eligible for registration as a pharmacist in Great Britain. The successful candidates will be expected to teach up to the standard of the Qualifying Examination of the Pharmaceutical Society of Great Britain.

The Ghana Government intends to establish Kumasi College of Technology as an autonomous University in the very near future, and teaching may then be up to General Degree level. In addition to teaching duties, the candidates will be expected to participate in a Research Programme of Investigation of the Medicinal and Toxic Plants of the Country. This programme is being carried out in conjunction with Chelsea College of Science and Technology.

Contract appointments are normally for five years, and may be renewed. Three months' notice of resignation of an appointment is required on either side. The contract salary scale is £1,063 15s. by £57 10s. to £1,868 15s. The entry point is fixed according to qualifications and experience. This salary scale is now under review. In addition, children's allowances are paid up to a maximum of three, and a gratuity at the end of the contract at the rate of £150 for each year of satisfactory service. The College is fully residential and members of staff are housed in pleasant modern bungalows on the spacious campus; climate and living conditions are good. Annual leave with three free return passages in four years is granted to members of staff and their families.

Application forms and an Information Brochure may be obtained from the Assistant Registrar, Kumasi College of Technology, 29 Tavistock Square, London, W.C.1, who will also be glad to answer any questions, either about the work of the School or about living conditions in Ghana.

ROYAL MILITARY COLLEGE OF Science, Shrivenham, Berkshire, requires Graduate Demonstrators (male) in Department of Electrical and Instrument Technology. Teaching at University level. To assist in supervision of Students' laboratory work and in research by Staff and Students. Extensive well-equipped laboratories. Opportunities to engage in personal research towards higher degree in fields of electrical engineering, electronics, computing and servo-mechanisms. Qualifications, first- or second-class honours degree or equivalent in electrical engineering or physics. Salary range: £754 to £910, superannuation under F.S.S.U. Appointments normally three years, but may be extended. Opportunities exist for promotion to grades of Lecturer and higher grades. Quarters available for single men; possibility of houses for married men.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting D.200/1A. Closing date May 13, 1961.

UNIVERSITY COLLEGE OF WALES

ABERYSTWYTH
DEPARTMENT OF ZOOLOGY

Applications are invited for the Chair of Zoology at a commencing salary of not less than £2,600 per annum.

Further particulars can be obtained from the Registrar. Ten copies of applications, together with the names of three referees, should be sent by May 20, 1961.

T. MAELGWYN DAVIES,
Registrar.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Assistant Lecturer or Lecturer in the Department of Zoology. The initial salary will be in the range £800 to £1,250 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than May 10, 1961, by the Registrar, The University, Liverpool, 3, from whom further particulars may be obtained, quoti[illegible] f: C.V/N.

LONDON COUNTY COUNCIL

SCIENTIFIC BRANCH

EXPERIMENTAL OFFICER, AND ASSISTANT EXPERIMENTAL OFFICER required at the Northern Outfall Works, Beckton, E.6. Duties involve chemical control of new plant and associated research.

Salaries: Experimental Officer, £750 to £1,140; Assistant Experimental Officer, £540 to £750.

Starting salaries according to age and experience. Experimental Officers must hold a pass degree including chemistry or H.N.C.; Assistant Experimental Officers a higher school certificate in chemistry or G.C.E. in five subjects including chemistry and one other scientific subject at advanced level or an equivalent qualification.

Apply Medical Officer of Health, (DI/A/N 1064/4), County Hall, London, S.E.1.

HUNTING TECHNICAL SERVICES LIMITED

require the following staff for overseas work for periods up to two years.

1. AGRONOMISTS

The work will mainly involve the establishment and management of crop trials. Experience in experimental technique is essential while a sound practical knowledge of irrigated crops such as rice and cotton is also important.

2. SOIL SURVEYORS

Minimum qualifications are a Science Degree and preference will be given to men with experience in soil survey abroad.

3. GEOLOGIST OR PHYSICIST

with experience in ground water hydrology. The work will involve drainage investigations including tube-wells.

4. CHEMIST

for analytical work in soils. Qualifications are a degree or its equivalent and preferably experience in soil analysis.

Salaries in each case will depend upon qualifications and experience. Accommodation will be provided together with generous local allowances. Please write to: Personnel Manager, Hunting Surveys Ltd., 6 Elstree Way, Boreham Wood, Herts.

UNIVERSITY OF MANCHESTER

Applications are invited for a Research Post (under the Agricultural Research Council) in the Department of Botany. Candidates should be graduates with qualifications in botany or biochemistry; the successful applicant will be required to work on the biochemistry of senescence in plant tissues. Facilities for studying for a higher degree are available. Salary £400 per annum.

Applications should be sent not later than May 13, 1961, to Dr. E. W. Simon, Department of Botany, the University, Manchester, 13.

H.M. CHEMICAL INSPECTORS OF FACTORIES: Ministry of Labour. Five pensionable posts for men or women normally at least 35 and under 40 on March 1, 1961 (with extension for regular Forces service and Overseas Civil Service). Duties include giving expert advice on questions which arise from administering Factories Acts. Qualifications: A.R.I.C., A.M.I.Chem.E., A.Inst.P., or first- or second-class honours degree in appropriate subjects. At least two years' relevant industrial experience desirable. Starting salary (Inner London) from £1,516 (at 35 or under) to £1,625 (at 37 or over). Scale maximum £2,015. Promotion prospects.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form, quoting S/5293/61. Closing date May 25, 1961.

Two exceptional opportunities with one of the largest producers of day old chicks in this country

GRADUATE MATHEMATICIAN, STATISTICIAN OR ECONOMIST

to apply automatic data processing techniques to various problems, both scientific and commercial, in several departments. Previous experience with an electronic computer, although preferable, is not essential, and persons graduating this summer will be considered for the position.

GENETICIST/BIOMETRICIAN to design and analyse experiments in a breeding programme. An Honours graduate is required, with research experience in genetics, animal or plant breeding. The person appointed will join a team already engaged in various aspects of research into poultry improvement.

Starting salaries are subject to negotiation and depend on qualifications and experience. Successful applicants will be eligible to join the company's contributory pension scheme.

Application forms from:

THORNBERS

THORNBER BROS. LTD.
(Dept. N) RESEARCH DIVISION (APPOINTMENTS)
MYTHOLMROYD · HALIFAX
YORKSHIRE

AMPEX

HEAD OF RESEARCH

Ampex Electronics Ltd., a member of the Ampex International Organisation, wishes to appoint a highly-qualified person to head its Research Department.

Ampex manufactures and markets a wide range of precision magnetic-tape recording and memory equipment which has many varied applications; military, educational, industrial, and research. In addition to product development and manufacture, the group devotes large sums each year to basic research.

Applications for the post are invited from Physicists and Electrical or Electronic Engineers with a first- or second-class honours degree who have a good record of successful personal research and suitable experience in the direction of research. A good mathematical background is essential and an existing knowledge of the field of magnetism is desirable but not essential.

The successful applicant will be required to take charge of and expand the Reading Research Department. He will initiate, conduct and report on fundamental investigations into transducers and particulate and other media applied to magnetic recording and other memory systems. Publication of suitable material is encouraged and facilities for liaison with other research groups in the U.S.A. and elsewhere will be provided. This is a senior appointment and the salary, which will be commensurate with qualifications and experience, will exceed £2,000 per annum.

Contributory Pension and Life Assurance Schemes.

Free Sickness Insurance.

Please write or telephone for an application form to:
THE PERSONNEL MANAGER,
AMPEX ELECTRONICS LTD.,
ARKWRIGHT ROAD,
READING, BERKSHIRE. Reading 84221.

AGRICULTURAL RESEARCH COUNCIL require an honours graduate in biochemistry or related subjects to work on biophysical problems concerned with eggs at the Low Temperature Research Station, Cambridge. Good knowledge of general chemistry and physics or physical chemistry, an interest in protein chemistry and research experience essential. Appointment in Scientific Officer (£738 to £1,222) or Senior Scientific Officer (£1,342 to £1,654) grade according to qualifications and experience. Superannuation under F.S.S.U. —Applications, with names of two referees, to Director of the Station, Downing Street, Cambridge within 14 days.

THE PATENT OFFICE

offers an interesting, well paid job with good prospects to suitably qualified men and women in congenial working conditions.

interest

You will be dealing with inventions from the whole world in your chosen subject. By its very nature the work will inevitably maintain your knowledge of science and technology completely up to date and will give you inside knowledge of new manufactures well ahead of the public at large.

salary

The training salary for the first two years is £793 and £824. On satisfactory completion the scale is £941–£1,719 by regular increments, but there is a jump in the scale to £1,324 five years after entry, or only four or even three in cases of special merit. Approved postgraduate experience fetches a higher starting salary. One promotion only, of which prospects are excellent, raises your maximum to £2,715. Reasonable proportion of still higher posts up to £3,865 all filled exclusively by promotions from entry grade.

qualifications

Age 21–35 and first- or second-class honours degree in physics, chemistry, engineering or mathematics, or an equivalent such as A.R.I.C., A.Inst.P., or corporate membership of I.C.E., I.Mech.E., or I.E.E., or first- or second-class honours Diploma of Technology.

conditions

Location, London, five-day week. Annual leave 4½ rising to 6 weeks. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information, or for a visit to the Patent Office to see the work, entirely without obligation. **The Superintending Examiner (B Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Telephone** HOLBORN 8721. **Ext.** 324.

CANADA

RESEARCH CHEMISTS

GRAIN RESEARCH LABORATORY
BOARD OF GRAIN COMMISSIONERS
WINNIPEG, MANITOBA

UP TO $7,860

To undertake independent research on problems relating to the Chemistry of wheat, flour, dough and related products.

Candidates must have a Doctor's or Master's degree and some related experience.

For details and application forms write in the first instance to:

Department 2154 DOA,
National Employment Service of Canada,
61 Green Street, London W.1

MIDDLESEX COUNTY COUNCIL
EDUCATION COMMITTEE
HENDON TECHNICAL COLLEGE
THE BURROUGHS, HENDON, LONDON, N.W.4

Principal: E. Williams, B.Sc., Ph.D., F.R.I.C.

This College, situated in pleasing surroundings only a few miles from the centre of London, is one with well-developed advanced courses. "Sandwich" courses are a feature of the college work. Due to the rapid development of advanced work an increasing number of men and women of ability and initiative are required as members of the full-time staff, and they are offered salaries as shown below.

ELECTRICAL ENGINEERING DEPARTMENT

Lecturer in Applied Physics. Applicants should be Physicists with special qualifications in Electronics. Applicants should be graduates with good industrial experience. Teaching experience, whilst being very desirable, is not essential. Corporate membership of the appropriate professional institutions is also very desirable. Salary within the range £1,408 to £1,601 per annum.

Anyone interested in the above post can obtain application forms and more information from the Clerk to Governing Body, Town Hall, Hendon, London, N.W.4.

C. E. GURR, M.Sc., Ph.D.
Chief Education Officer.

UNIVERSITY OF SYDNEY
CHAIR OF PHYSICS (HIGH ENERGY NUCLEAR PHYSICS)

Applications are invited for the Chair of Physics (High Energy Nuclear Physics). The Professor will be in charge, under the general administration of the Head of the School of Physics, of the various branches of High Energy Nuclear Physics, as well as of those members of staff whose work lies mainly in this field. Salary will be at the rate of £A.4,250 per annum, plus cost of living adjustments (at present £A.36 per annum). There is retirement provision under either the Sydney University Professorial Superannuation Scheme or the New South Wales State Superannuation Scheme. Under the Staff Members' Housing Scheme, in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house. The Senate reserves the right to fill the Chair by invitation.

A statement of the Conditions of Appointment and Information for Candidates may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close in Australia and London, on June 30, 1961.

MEDICAL RESEARCH COUNCIL

Applications are invited from Veterinary Surgeons, preferably in the 25-32 age group, for a post in the Biological Standards Control Laboratory, Hampstead, N.W.3. Duties will be primarily to assist in the control of virus vaccines, but time will be available for research.

Applications, with full details and names of two professional referees, should be sent to the Director, National Institute for Medical Research, The Ridgeway, Mill Hill, N.W.7.

UNIVERSITY OF BIRMINGHAM
DEPARTMENT OF BOTANY

Applications are invited for the post of Lecturer (£1,050 by £50 to £1,400 by £75 to £1,550; £1,550 by £75 to £1,850) or Assistant Lecturer (£800 by £50 to £950) in the Department of Botany. Preference will be given to candidates with an interest in the fields of mycology and plant pathology. The appointment will be made from October 1, 1961, or earlier, if possible, and will carry F.S.S.U. and family allowance benefits. Initial stipend will be related to qualifications and experience.

Applications (three copies), naming three referees, should be sent by May 15, 1961, to the Assistant Registrar (Science), The University, Edgbaston, Birmingham, 15, from whom further particulars may be obtained.

UNIVERSITY OF LONDON
GOLDSMITHS' COLLEGE
TRAINING DEPARTMENT

Applications are invited for the post of Lecturer or Senior Lecturer in Botany in the Training Department. Qualified to lecture in Plant Physiology in degree courses. Full-time appointment preferred, but part-time would be considered. Salary on Pelham scale for Lecturers in Training Colleges.

Applications (five copies) to the Warden, Goldsmiths' College, New Cross, London, S.E.14, from whom further particulars can be obtained.

CITY OF PORTSMOUTH
COLLEGE OF TECHNOLOGY
DEPARTMENT OF MATHEMATICS AND PHYSICS

Applications are invited for the posts of (a) Senior Lecturer in Theoretical Physics; (b) Lecturer in Mathematics. Salary scales (a) £1,550 to £1,750; (b) £1,370 to £1,550.

Further particulars and application forms, to be returned by May 20, 1961, may be obtained from the Registrar, College of Technology, Portsmouth.

UNIVERSITY COLLEGE
IBADAN, NIGERIA

Applications are invited for post of Senior Technician in Department of Botany. Appointment commencing October, 1961. Salary scale: £1,050 by £25 to £1,100 (bar); £1,150 by £50 to £1,400 per annum. Passages paid for appointee, wife and up to five children under 11 years, on appointment, annual leave and termination. Part-furnished accommodation at rent not exceeding 7.7 per cent of salary. Children's, car and outfit allowances. Pension scheme.

Detailed applications (six copies), naming three referees, by May 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

NATURAL RUBBER PRODUCERS' RESEARCH ASSOCIATION

PHYSICISTS and CHEMISTS

The Natural Rubber Producers' Research Association require physicists and chemists to undertake research on polymers. The appointments are especially suited to those wishing to make their career in research. Candidates should possess a good honours degree, some research experience would be advantageous but it is not essential. A high level of ability and enthusiasm is sought, and successful applicants will be given every encouragement, including a liberal publication policy, to show initiative and responsibility. Salary initially will be within the range £760 to £1,695 according to age, qualifications and experience, with superannuation under the F.S.S.U. scheme, and an allowance for children. Pleasant working conditions in laboratories located about 20 miles north of London.

Please write to the Director of Research, 48-56 Tewin Road, Welwyn Garden City.

Candidates from overseas should include full details with their application.

SCIENTIFIC LIAISON — JAPAN

Unique opportunity for Physicist or Physical Chemist with broad scientific interests and excellent command of the Japanese language.

Major American Company has available a stimulating scientific liaison position in Japan. Strong emphasis on basic science. Period of assignment in Japan three to five years.

Reply to Box 962, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

AUSTRALIAN NATIONAL UNIVERSITY

INSTITUTE OF ADVANCED STUDIES

POSTS IN THEORETICAL PHYSICS

Applications are invited for appointments as Senior Fellow and Senior Research Fellow in the Department of Theoretical Physics, which is carrying out theoretical studies in nuclear physics, in the physics of elementary particles and in plasma physics. Preference will be given to applicants with experience in elementary particle physics. The present academic staff of the Department are: Professor K. J. Le Couteur, Dr. D. C. Peaslee, Dr. F. C. Barker, Dr. L. J. Tassie, Dr. B. Robson and Dr. K. Kumar. The salary range for Senior Fellows is £A.2,592 to £A.3,102. Appointment is for an initial period of five years; thereafter it may be made permanent. A Senior Fellow is entitled to one year's study leave on full pay, plus a contribution towards travel and other expenses, in every six years. The salary range for Senior Research Fellows is £A.2,272 to £A.2,752. Appointment is for three years, with possible extension to a maximum of five years. Salaries in the University are under review. Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid and assistance with housing is provided.

A summary of condition of appointment is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 26, 1961.

CHEMICAL SOCIETY. AN EDITORIAL Assistant is required for preparation and proofing of *Current Chemical Papers*. Applicants, who may be men or women, should have a good honours degree in chemistry, as the work requires an understanding of modern chemical research, and they should be able to translate simple technical German and French. Salary in the range £600, rising by £50 per annum to £1,250 per annum, beginning according to qualifications.—Applications, not later than May 15, to the Editor, The Chemical Society, 38 York Terrace, London, N.W.1, from whom further particulars may be obtained.

A VACANCY EXISTS FOR A SCIENTIFIC Assistant to work on literature for *Nutrition Abstracts and Reviews*. Applicants should possess an honours degree or its equivalent in biological sciences, preferably including physiology, and an ability to write correct English. Knowledge of languages, especially Spanish, would be advantageous. Scale £690 to £1,750, with starting salary according to age, qualifications and experience. Superannuation under F.S.S.U.—Applications, giving referees, by May 20, 1961, to the Director, Commonwealth Bureau of Animal Nutrition, Rowett Research Institute, Bucksburn, Aberdeen.

MIDDLESEX COUNTY COUNCIL EDUCATION COMMITTEE

BRUNEL COLLEGE OF TECHNOLOGY

Woodlands Avenue, Acton, W.3

Principal: Dr. J. Topping, M.Sc., D.I.C., F.Inst.P.

DEPARTMENT OF CHEMISTRY

Applications are invited for the following posts as from September 1, 1961:

LECTURER IN ZOOLOGY AND GENERAL PHYSIOLOGY

To teach particularly Vertebrate Zoology and General Physiology in Diploma in Technology courses, part-time degree and professional courses.

ASSISTANT LECTURER, GRADE B, IN GENERAL PHYSIOLOGY AND ZOOLOGY

To teach Invertebrate Zoology and some Physiology in Diploma in Technology, part-time degree and professional courses.

Candidates for both posts should hold a good honours degree and have appropriate teaching, industrial or research experience.

Salary within the range:

Lecturer, £1,408 to £1,601 per annum.

Assistant Lecturer, Grade B, £828 to £1,486 per annum according to age and experience.

Application forms, available from the Principal, to whom completed applications should be returned within fourteen days of the appearance of this advertisement.

C. E. GURR, M.Sc., Ph.D., Chief Education Officer.

UNIVERSITY COLLEGE OF WALES

WELSH PLANT BREEDING STATION

PLAS GOGERDDAN

Near ABERYSTWYTH

Applications are invited for appointment to a vacancy for an Assistant Experimental Officer at the Station. The vacancy is in the Developmental Genetics Section, and the work is concerned primarily with recording and handling of genetical material. Applicants should be graduates in agriculture or botany or horticulture, or seek to graduate in the summer of 1961. Salary on the scale £450 10s. at age 18 to £983 maximum.

Applications in writing, with the names of two referees, to the Secretary before May 31, 1961.

NIGERIAN COLLEGE OF ARTS, SCIENCE AND TECHNOLOGY

ENUGU BRANCH

Applications are invited for the following: (a) Senior Lecturer Grade II or Lecturer in Land Surveying; (b) Senior Lecturer Grade I or II in Physics; (c) Senior Lecturer Grade II or Lecturer in Mathematics; (d) Lecturer in Geography. Qualifications: (a) Fellow or Associate Member of R.I.C.S. or similar qualification. (b) (c) and (d) Good Honours degree and Teaching experience. Date of commencement of duties: Last week of September, 1961. Contract salary scales: Senior Lecturer, Grade I, £2,220 to £2,445 per annum; Senior Lecturer, Grade II, £1,440 to £1,824 per annum; Lecturer, £792 to £1,760 per annum (plus inducement addition £180 to £300 per annum in the case of Lecturer and Senior Lecturer, Grade II, for overseas appointees), and gratuity of £25 to £37 10s. for each completed three months' residential service. Entry point according to qualifications and experience. Tours from 10 to 18 months. Free passages including wife. Children's U.K. maintenance grant up to £150 per annum and passages assistance. Partly furnished quarters at one-twelfth basic salary rental.

Applications (eight copies), giving age, qualifications, experience and names of three referees, should be sent to the Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2, by May 12, 1961.

UNIVERSITY OF AUCKLAND

NEW ZEALAND

SENIOR LECTURESHIP OR LECTURESHIP IN CIVIL ENGINEERING

Applications are invited for the above-mentioned post. Candidates should be university graduates in Civil Engineering, with, preferably, a higher degree and/or professional experience. Previous professional or academic experience in the Theory of Structures would be an added advantage. The salary scale for a Senior Lecturer is £1,750 per annum rising to £2,000, and for a Lecturer £1,250 per annum rising to £1,700. Commencing salary within the appropriate scale will be determined according to qualifications and experience. An allowance is made towards travelling expenses.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in New Zealand and London, on June 15, 1961.

UNIVERSITY OF HONG KONG

LECTURESHIP IN BOTANY

Applications are invited for the above-mentioned post. Preference will be given to applicants with experience in plant physiology or developmental anatomy, but persons experienced in other branches of Botany should also apply. Annual salary (superannuable) is: £1,575 by £50 to £2,175 (man) or £1,200 by £40 to £1,680 (woman). There is also an expatriation allowance of £225 a year if applicable. Salaries are under review. The equivalent of income tax in the Colony is comparatively low. First-class sea passages are provided for expatriate staff and their families on first appointment and leaves. Accommodation at reasonable rental is provided for those receiving expatriation allowance.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Hong Kong and London, on June 2, 1961.

UNIVERSITY COLLEGE OF GHANA

Applications are invited from suitably qualified graduates for Research Fellowship in the Division of Soil Science of the Faculty of Agriculture. Salary scale (under review) £G.1,000 by £G.50 to £G.1,350 (bar) by £G.75 to £G.1,800; £G.1,850 per annum. Entry point according to qualifications and experience. F.S.S.U. Outfit, family and other allowances. Passages for appointee and family on appointment, leave and normal termination. Part-furnished accommodation at a charge not exceeding 7.5 per cent of salary.

Detailed applications (six copies), naming three referees, by May 30, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

UNIVERSITY OF ABERDEEN

DEPARTMENT OF PHYSIOLOGY

Applications invited for: A Senior Research Fellowship, salary not less than £1,100 per annum, plus F.S.S.U. A Junior Research Fellowship, salary within the range £800 to £950 per annum, plus F.S.S.U. Both appointments, which are financed by the U.S. Public Health Service, are for three years, beginning on September 1 or a date to be arranged. The Fellows will form a team, led by Dr. H. W. Kosterlitz, to investigate the mechanism of the action of morphine and other analgesics on the peripheral autonomic nervous system. One Fellow should have some experience in pharmacological techniques and the other in neurophysiological techniques.

Further details and forms of application may be obtained from the Secretary, Marischal College, Aberdeen, to whom applications (three copies), giving details of qualifications, etc., and the names of two referees, should be submitted by May 27, 1961.

INDEX BIOLOGICUS

Executive Editor required for periodical providing scientific information service in biological fields. Organizing ability, knowledge of indexing principles, including mechanical methods, wide scientific interests, and experience of press work are all desirable qualifications for the post, and the salary will be determined accordingly. Place of work will be in London or Oxford.

Please reply, giving full details of qualifications and experience, to the Managing Director, Pergamon Press Limited, 4 & 5 Fitzroy Square, London, W.1.

GEOPHYSICISTS: DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH. Two pensionable posts (graded as Geologist or Senior Geologist) in Geological Survey and Museum, London, for men at least 21 on July 1, 1961. Duties are concerned with geophysical surveys in the field. Candidates should normally have (or obtain in 1961) first- or second-class honours degree in geology, geophysics, physics, or mathematics, together with a university qualification, to at least first year standard in geology and in physics or mathematics, or an equivalent qualification. Experience in applied geophysics an advantage. At least three years' postgraduate or other approved experience necessary for appointment as Senior Geologist. Inner London salary within the scales £793 to £1,282 or £1,402 to £1,719, according to age, qualifications and experience. Starting pay may be above minima. Promotion prospects.—Write Civil Service Commission, 17 North Audley Street, London, W.1, for application form, quoting **S/5298/61.** Closing date May 18, 1961.

NATIONAL COLLEGE OF FOOD TECHNOLOGY

ST. GEORGE'S AVENUE, WEYBRIDGE

Principal: J. D. Mounfield, M.Sc.Tech., Ph.D., F.R.I.C.

LECTURER IN PHYSICS

Applications are invited for the post of Lecturer in the College from graduates in physics or chemical engineering. The duties will be mainly concerned with postgraduate and four-year sandwich courses in food technology. Facilities for research are available. Salary scale: £1,370 by four at £35 and one at £40 to £1,550 per annum. Starting salary dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

THE METAL BOX COMPANY LIMITED
RESEARCH DEPARTMENT

A vacancy exists in the Analytical Section of the Research Department for a

GRADUATE CHEMIST

to take over investigations into the extractability of minor constituents of packaging materials by foods. The exploration of these problems presents very considerable difficulties and requires the use of the whole range of methods developed by modern analytical chemistry. A primary interest in analytical research is therefore essential. Interpretation of the results will require a full understanding of the work going on in many centres in this country and abroad. Excellent equipment and considerable experience are available to support the investigations.

Applicants, men or women, should have an Honours Degree in Chemistry or should hold an equivalent qualification. A Higher Degree and/or further research experience would be highly desirable.

Please apply to: Ref. Chem. 9, Administration, Research Department, **THE METAL BOX CO. LTD.**, Kendal Avenue, Westfields Road, Acton, London, W.3.

NATIONAL COLLEGE OF FOOD TECHNOLOGY

ST. GEORGE'S AVENUE, WEYBRIDGE

Principal: J. D. Mounfield, M.Sc.Tech., Ph.D., F.R.I.C.

LECTURER IN CHEMISTRY

Applications are invited for the post of Lecturer in the College from graduates in Chemistry or Biochemistry. The duties will be mainly concerned with postgraduate and four-year sandwich courses in food technology. Facilities for research are available. Salary scale: £1,370 by four at £35 and one at £40 to £1,550 per annum. Starting salary dependent on qualifications and experience.

Application forms (obtainable from the College) should be sent to the Principal as soon as possible.

ONTARIO CANCER FOUNDATION

HAMILTON CLINIC
HAMILTON GENERAL HOSPITAL, HAMILTON, ONTARIO

Applications are invited for appointment as Clinical Physicist. Applicants should possess at least an honours degree in physics or equivalent. Some experience in hospital physics is desirable but not necessary. An interest in research in clinical physics or radiobiology is expected. Minimum initial salary for untrained honours graduate is $5,000 per annum; pension scheme.

Applications should be sent to the undersigned, from whom further details may be obtained.

R. J. HORSLEY,
Senior Physicist.

THE BRITISH OXYGEN COMPANY Limited have a vacancy in the Information Section of their Scientific Division for a graduate in science or engineering. The work includes abstracting and literature searching and covers a wide range of subjects.—Applicants should write to the Administration Manager, The British Oxygen Company Ltd., Scientific Division, Deer Park Road, London, S.W.19.

UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND

Applications are invited for (A) Lectureship or (B) Assistant Lectureship in Mathematics. Salary scales: (A) Grade I, £1,600 by £50 to £1,900 per annum. Grade II, £1,350 by £50 to £1,600 per annum. (B) £1,200 by £50 to £1,350 per annum. Passages to Salisbury for appointee, wife and dependent children on appointment, with allowance for transport of effects. Superannuation and Medical Aid Schemes. Unfurnished accommodation at rent of 15 per cent of salary. Assistance given for triennial visits overseas.

Detailed applications (six copies), naming three referees, by May 25, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

PEMBURY HOSPITAL

PEMBURY, KENT

Technician required to assist the Physicist attached to the Radiotherapy Department. Whitley Council Salary and Conditions.

Applications, stating qualifications and experience of applied physics, with the names of two referees, should be addressed to the Surgeon Superintendent.

UNIVERSITY OF SHEFFIELD

Through the generosity of Batchelors Foods Ltd., The University offers a Research Fellowship in Biochemistry or Microbiology tenable from October 1, 1961, and open to graduates of any British University. The Fellowship will be tenable initially for a period of two years and may be extended for a third year. Value £450 a year. The Fellow will be required to pursue a full-time course of research in the University of Sheffield under conditions approved by the Head of the Department concerned.

Applications (two copies), including the names and addresses of referees and, if desired, copies of testimonials, should reach the Registrar (from whom further particulars may be obtained) by May 20, 1961.

UNIVERSITY COLLEGE OF SWANSEA

Applications are invited for a Lectureship in Chemical Engineering. Salary on the scale £1,050 to £1,850 per annum. Membership of F.S.S.U. and children's allowance scheme.

Further particulars may be obtained from the Registrar, University College, Singleton Park, Swansea, to whom applications (six copies) must be sent by May 20, 1961.

UNIVERSITY COLLEGE OF WALES

ABERYSTWYTH

Applications are invited for the post of Assistant Lecturer in the Department of Applied Mathematics, to take up duties on October 1, 1961.

Further particulars and forms of application can be obtained from the Registrar, to whom applications should be sent not later than May 20, 1961.

AGRICULTURAL RESEARCH COUNCIL require an honours graduate in organic or physical chemistry at the Low Temperature Research Station, Cambridge, to work initially on problems concerned with flavour and odour in meat and bacon. Some research experience desirable but not essential. Appointment in Scientific Officer (£738 to £1,222) or Senior Scientific Officer (£1,342 to £1,654) grade according to qualifications and experience. Superannuation under F.S.S.U.—Applications, with names of two referees, to Director of the Station, Downing Street, Cambridge.

NATIONAL PHYSICAL LABORATORY, Teddington, Middlesex, require Senior Scientific Officers/Scientific Officers in Acoustics Section of Applied Physics Division. (a) To investigate methods of noise measurement. Supervision of measurements in field and control of subjective listening experiments. Experience in statistics, applied psychology, or electronics useful. (b) To improve standards of instrumentation of sound measurement at audio-frequencies. Classical physicist with interest in instrument design suitable. Qualifications. First- or second-class honours science degree or equivalent. For senior post three years' postgraduate research experience required. Minimum age 26. Salaries: Scientific Officer, £773 to £1,267; Senior Scientific Officer, £1,392 to £1,714. Starting point dependent upon experience.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting A.148/1A. Closing date May 24, 1961.

MINISTRY OF AGRICULTURE, FISHERIES AND FOOD

SCIENTIFIC RESEARCH FELLOWSHIP

Applications are invited for Scientific Research Fellowships (three years) value £1,325 to £1,640 (Senior) and £910 to £1,220 (Junior) in the following range of subjects: (1) At the Royal Botanic Gardens, Kew: The study of living plants in association with the Herbarium collection. (2) At the Fisheries Laboratory, Lowestoft: Radio ecology of aquatic animals and plants. (3) At the Veterinary Laboratory, Weybridge: Study of the methods of progesterone assay and metabolism in ruminants. Qualifications: normally first- or second-class honours degree; evidence of a high standard of ability in research and at least two years' postgraduate research experience (three years for Senior Fellowships). No age limits. F.S.S.U.

Write Room 612, Ministry of Agriculture, Fisheries and Food, Great Westminster House, Horseferry Road, London, S.W.1, for application form.

ROYAL UNIVERSITY OF MALTA

Applications are invited for the Chair of Physics. Salary £1,900 per annum (including overseas allowance). F.S.S.U. Passages provided for appointee, wife and children under 12 years on appointment and normal termination. Duties to be assumed as soon as possible.

Detailed applications (eight copies), naming three referees, as soon as possible to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

THE AGRICULTURAL RESEARCH COUNCIL require an honours graduate in chemistry or biochemistry at the Low Temperature Research Station, Cambridge, to work on a project supported by United States Counterpart funds. Appointment for a period of about three years to investigate fundamental aspects of the dehydration of meat. Subject for study is of a type generally suitable for submission as a dissertation for a higher degree. Salary according to qualifications in the range £738 to £1,222. Superannuation under F.S.S.U.—Applications, with names of two referees, to Director of the Station, Downing Street, Cambridge.

UNIVERSITY OF READING

CHIEF TECHNICIAN (GRADE I)

Applications are invited for the post of Chief Technician in the Department of Zoology. The successful applicant will be required to take charge of the technical staff and services in the department, and to assist with planning in connection with a proposed new building.

Salary scale £895 by £30 to £1,015, and in special cases up to £1,150 per annum.

Further particulars from the Assistant Bursar, The University, Reading.

UNIVERSITY COLLEGE OF GHANA

Applications are invited from Chemists, Physicists or Biologists for two posts of Research Fellowships in the Physics Department. The work will be in connection with Health Physics and Radioisotope Unit. Applicants will be required to undertake research using various radio-tracer methods into a variety of problems in Ghana. Some lecturing may be required. Experience in use of isotopes is desirable. Salary scale (under review) £G.1,000 by £G.50 to £G.1,350 (bar) by £G.75 to £G.1,800; £G.1,850 per annum. Entry point according to qualifications and experience. F.S.S.U. Outfit, family and other allowances. Passages for appointee and family on appointment, leave and normal termination. Part-furnished accommodation at a charge not exceeding 7·5 per cent of salary.

Detailed applications (six copies), naming three referees, by June 10, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

CHEMICAL RESEARCH TECHNICIAN/Assistant to work on Steroids with team investigating endocrinology in relation to human biology and genetics. Salary Whitley Scale.—Apply, giving two referees, to Dr. J. M. Tanner, Institute of Child Health (University of London), The Hospital for Sick Children, W.C.1.

BASUTOLAND

PIUS XII UNIVERSITY COLLEGE LECTURESHIP OR ASSISTANT LECTURESHIP IN BOTANY

Applications are invited from suitably qualified persons for the post of Lecturer or Assistant Lecturer in Botany at this small, but strongly developing, College. Basutoland offers exceptionally interesting research opportunities to Botanists specializing in systematics and ecology. This post would be specially suitable for someone who would be willing to devote five or six years of his academic career to the education of Africans, and who is seeking an opportunity for original research. Appointment tenable from February 1, 1962. Salary scale for Lecturer: £1,000 by £50 to £1,250 (efficiency bar) by £50 to £1,550; for Assistant Lecturer: £720 by £40 to £960. Status and initial salary according to qualifications and experience. Pension scheme. Family allowance of £100 per annum, plus £40 per child under the age of 18. Train and sea passages arranged for appointee, wife and children. Baggage allowance.

Further information and application forms, to be returned by June 15, obtainable from the Registrar, Pius XII College, Roma, Basutoland, Southern Africa.

A YOUNG FEMALE GRADUATE CAPABLE of carrying out vitamin analyses on biological materials is required. Postgraduate experience is desirable, and a knowledge of chromatographic methods would be valuable. The successful candidate will be required to assist in an existing nutritional research programme, but the position allows considerable scope for individual initiative. – Full written applications should be addressed to the Chief Chemist, Bob Martin Limited, Southport, Lancashire.

BIOCHEMIST. A MALE GRADUATE with some years' experience is required by the Research Laboratories of the British Drug Houses Ltd. The work is concerned mainly with the identification and assay of drug metabolites and with aspects of protein chemistry. The Company offers good conditions, including a Superannuation Fund with Life Assurance and Profit Sharing Scheme.—Applications, with full details, to Personnel Manager, Ref. HAC/VP, The British Drug Houses Ltd., Graham Street, N.1.

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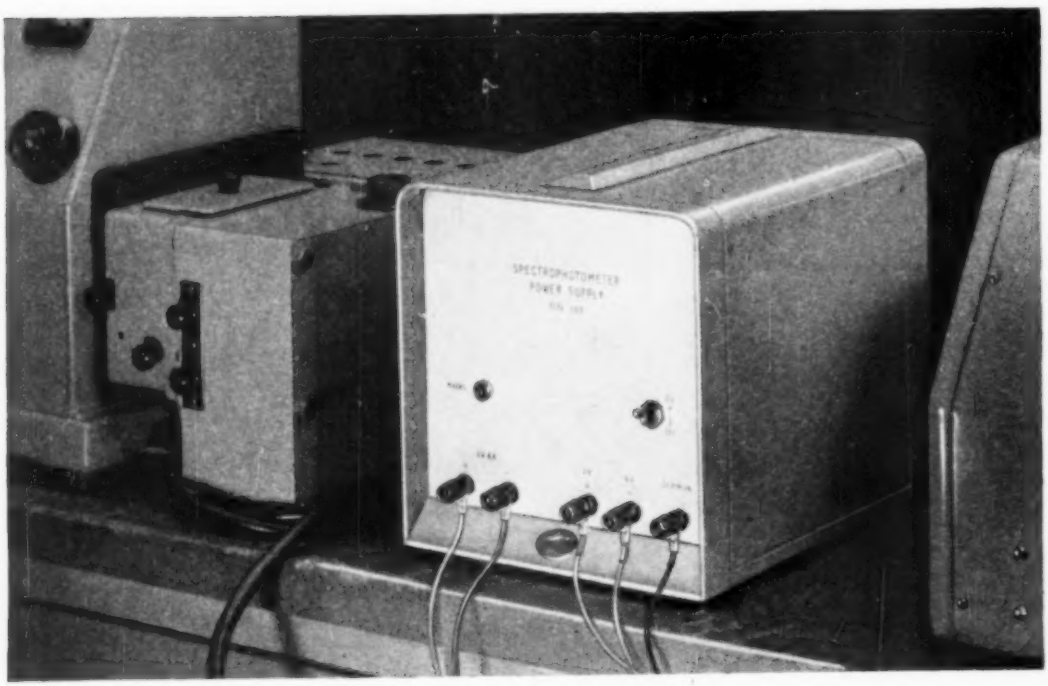

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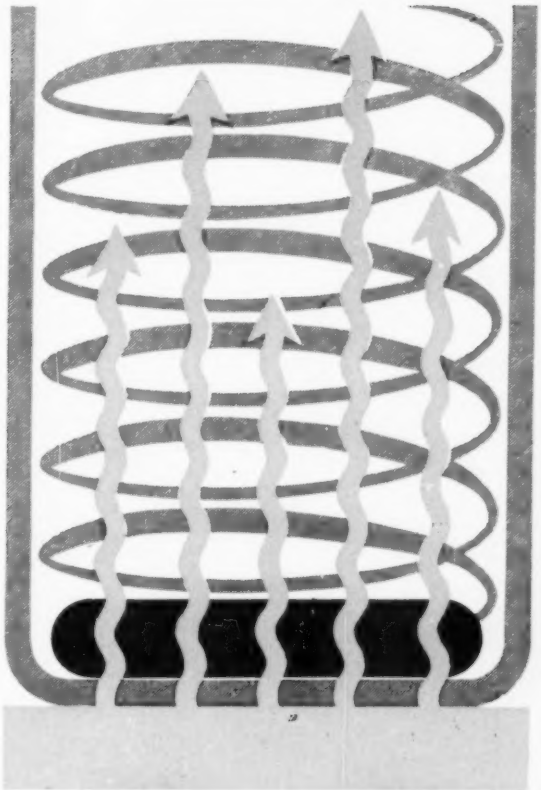

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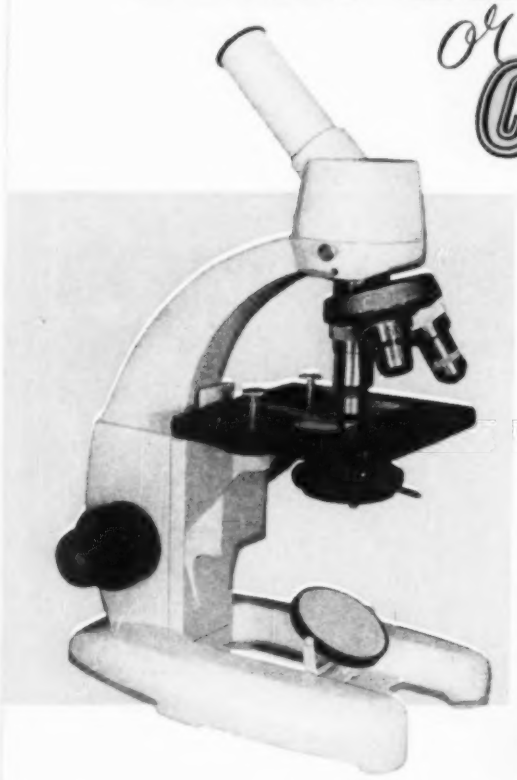

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